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Case Report

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Clinical condition of patients with Obesity Hypoventilation Syndrome (OHS): case report

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Abstract: Obesity hypoventilation syndrome (OHS) or Pickwikian's syndrome consists of obesity, breathing-related sleep disturbances, and chronic daytime hypoventilation. Identifying OHS is essential due to the risk of clinical exacerbation leading to respiratory failure and the high mortality rate among untreated patients. A 55-year-old woman was admitted to the emergency room with two days of weakness and fatigue. She is unable to perform daily tasks due to shortness of breath. She was recently diagnosed with diabetes. The patient weighs 133 kilograms and has a height of 155 centimeters (Body Mass Index of 55,4 kg/m2). The patient's blood glucose was 351 mg/dl, with an abnormal result of HbA1C of 11.5%. The blood pressure tends to stage 1 hypertension, and arterial blood gas examination showed respiratory acidosis. We diagnosed her with obesity hypoventilation syndrome, type 2 diabetes, and stage 1 hypertension. During her five-day hospitalization, her condition improved. Correct diagnosis and management can improve the patient's quality of life and decrease the risk of comorbidities

Keywords: Cardiometabolic, Diabetes Mellitus, Hypertension, Obesity, Obesity Hypoventilation Syndrome

INTRODUCTION

Overweight and obesity represent an abnormal or excessive accumulation of fat that poses a health risk. Body mass index (BMI) is used to measure personal nutritional status. In the asian population, overweight is defined as BMI between 23-24,9 kg/m2, and obesity is a BMI of more than 25 kg/m2.[1] Southeast asian population, the prevalence of overweight and obesity tends to increase; previously, from 8% to 30% in the male population and from 8% to 52% in the female population.[1,2] The proportion of people with BMI >27 kg/m2 in the Indonesian population increased from 10.5% in 2007 to 21.8% in 2018.[1,3]

People with obesity correlate with cardiometabolic and respiratory disease. Obesity can trigger medical conditions known as obesity hypoventilation syndrome (OHS).[1,4,5] The prevalence of OHS is unknown in Indonesia or other countries due to a lack of population-based studies. However, the prevalence of OHS can be estimated at 0.15% to 0.3% in the United States.[6,7] Obesity hypoventilation syndrome (OHS) or Pickwikian's syndrome is a group of symptoms consisting of obesity, breathing-related sleep disturbances, and chronic daytime hypoventilation; after ruling out

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other causes of hypoventilation, such as pulmonary disease, chest wall deformity, hypothyroidism, or neuromuscular disease.[6,8]

Identifying obesity hypoventilation syndrome is vital because of the possibility of clinical exacerbation leading to respiratory failure and the high mortality rate in untreated patients. Symptoms of arterial hypertension and insulin resistance are more common in patients with OHS.[7,9] Comorbidities such as heart failure, coronary artery disease, and cor pulmonale are more common in patients with OHS, and the likelihood that such patients will require invasive mechanical ventilation or ICU admission is also increased. Patients with OHS use more healthcare resources.[6,7]

CASE REPORT

A 55-year-old woman was admitted to the emergency room with two days of weakness and fatigue. She also experiences nausea and dizziness. She is unable to perform daily tasks due to shortness of breath. Before she went to the hospital, she had experienced this symptom for an extended period of time. There is no illness comparable to cough, fever, and influenza. She was recently diagnosed with diabetes and began taking metformin 500 mg three times a day and glimepiride once daily. The patient has no asthmatic medical history and has never smoked.

On the physical examination, the patient looked at compos mentis respiratory rate of 24 times per minute and peripheral oxygen saturation of 96% in room air, which escalated to 99% after using a nasal cannula with 3 liters of oxygen per minute. Patient's blood pressure of 116/66 mmHg, and heart rate of 97 bpm. A pulmonary examination revealed normal condition and typical heart sound. Both legs were edema. The patient's weight is 133 kg, and a height of 155 cm (Body Mass Index 55.4 kg/m2). She had fat accumulation on the neck, chest, and abdomen. However, the patient was not measured for neck, chest, and abdominal circumstances.

According to anteroposterior chest radiography, had been an increase in broncho vascular pattern and cardiomegaly. The patient's ECG result was normal sinus at 97 bpm (Table 1). To rule out a COVID-19 diagnosis, our physician did a COVID-19 PCR which showed a negative result. The patient's blood glucose was 351 mg/dl, with an abnormal result of HbA1C of 11.5%. Slightly increase in ALT liver function of 43U/L (normal: <31 U/L), normal kidney function, and creatinine of 0.58 mg/dL. Troponin results were negative. Normal Hemoglobin (15.6 g/dl), erythrocyte of 5.36 /µL, leucocyte of 7.630/µL, thrombocyte of 226.000/µL Arterial blood gas analysis (ABGA) was conducted after using a nasal cannula with pH 7.356, PaCO2 of 30.7 mmHg, PaO2 194.5 mmHg, Bicarbonate (HCO3) of 17.4 mmHg, base excess of -6.2 mmol/L (Table 2).

Table 1. Diagnostic Test Results

Diagnostic Test	Results
Chest X-ray Antero Posterior	Increased broncho vascular pattern and cardiomegaly
Electrocardiography	Early on the Emergency ward : • Normal sinus rhythm 97 bpm After hospitalized : • Normal sinus rhythm 86 beats bpm, left ventricle hypertrophy with occasional premature ventricular complex and prolonged QT interval
Echocardiography	Impaired systolic LV function 48%, hypokinetic cardiac muscle in segment anteroseptal and anterior, and abnormal diastolic LV function

We consult patients with internists, cardiologists, and pulmonologists. She was diagnosed with obesity hypoventilation syndrome with type 2 diabetes and stage 1 hypertension. She was treated in the High Care Unit (HCU). Treatment at HCU lasted for three days. The patient improved her shortness of breath, although she still had to use nasal oxygenation at 3 liters per minute. The patient's respiratory rate each day is between 18-22 times per minute. The patient's blood pressure fluctuated during treatment, systolic was recorded between 115-149 mmHg, and diastolic was recorded at 80-95 mmHg. Electrocardiography examination on day 2 of HCU treatment showed a normal sinus rhythm of 86 beats per minute with occasional premature ventricular complex and prolonged QT interval. The echocardiogram revealed abnormal Left ventricular systolic function of 48%, hypokinetic cardiac muscle in the anterior and anteroseptal segments, and abnormal Left ventricular diastolic function.

The patient used to take two types of oral antidiabetic drugs, namely metformin, and glimepiride, since being diagnosed with type 2 diabetes mellitus. However, the drug was discontinued and replaced with insulin administration by our internist. This replacement therapy has obtained the patient's consent. At the beginning, the patient received eight units of rapid-acting insulin therapy three times a day. The dose of rapid-acting insulin is tapered up to 22 units. The examination results (Table 4) showed increasing doses of rapid-acting insulin followed by decreased blood glucose levels. Our cardiologist also gave her furosemide IV and carvedilol 6.25 mg tablet once daily for her hypertension. The patient received supervision from a pulmonologist and got IV ceftriaxone therapy twice daily for five days of treatment in the hospital. In addition to receiving drug therapy to improve the patient's clinical condition, our internist also regulates the patient's diet by limiting the intake of calories to 1900 kilocalories per day with foods that are low in salt.

After five days of hospitalization, the patient went home in good condition by continuing therapy, such as a rapid-acting insulin dose of 10 units in the morning. The patient was administered 22 units of Rapid action insulin daily, 10 mg of amlodipine orally once daily, and 6.25 mg of carvedilol orally once daily. She was asked to change her lifestyle to be healthier by losing weight according to the ideal body mass index, taking medication regularly, and consuming foods low in fat and salt.

Table 2. Inpatient Laboratory Test Results

Laboratory Test	Results	Normal Value
Blood Glucose	351	<140 mg/dl
HbA1C	11.5	<5.7 %
Troponin I	0.004	<0.002
SGPT	34	<31 U/L
BUN	4.3	9.81-20.1
Creatinin	0.58	0.50-0.90
Natrium	136	136-146 mmol/L
Kalium	3.6	3.5-5.1 mmol/L
Chloride	103	98-106 mmol/L
Albumin	3.77	3.5-5.0 g/dL
Haemoglobin	15.6	12-16 g/dL
Erythrocyte	5.360.000	4.0-5.0 /uL
Leukocyte	7.630	5.0-10 /uL
Thrombocyte	226.000	150.000-450.000 /uL

DISCUSSION

The pathophysiology of OHS is related to three primary mechanisms: 1) obesity-related changes in the respiratory system, 2) alterations in respiratory drive, and 3) breathing abnormalities during sleep. Identifying one predominant or a combination of these critical mechanisms in a patient is crucial to characterize the OHS phenotype.[10] Obesity's nutritional status is a prominent clinical feature of this patient. The patient weighs 133 kg with a height of 155 cm (body mass index 55.4 kg/m2). According to the WHO western pacific region, the patient's BMI is classified as Obesity II (BMI> 30 kg/m2).[11] The incidence of OHS increases significantly, with a reported prevalence of nearly 50% of hospitalized patients with a BMI greater than 50 kg/m2. Obesity, especially severe, can be associated with significant changes in lung mechanics and respiratory muscle performance, causing significant reductions in total lung capacity, vital capacity, functional residual capacity, and increased residual volume.[5] It can lead to severe hypoxemia, hypercapnia, and other complications.[12] Clinically, patients with OHS may present with unexplained hypoxemia or symptoms such as excessive daytime sleepiness, fatigue, loud habitual snoring, nocturnal choking episodes, morning headaches, lower extremity edema, and low oxygen saturation.[6,12]

On physical examination, fat accumulated in the neck, chest, and abdomen. However, the clinician did not measure the neck, chest, and abdominal circumference. We recognize this as deprivation in our report. Patients with OHS are prone to have greater neck circumstances. The greater the neck circumstance is, the easier the upper airway may collapse. Obesity predisposes the upper airway to closure by reducing the pharyngeal size and enhancing collapsibility.[10,12,13]

The patient's respiratory rate reaches 24 breaths per minute, and we provide oxygen therapy with a nasal cannula of 3 liters per minute. Increased oxygen demand, followed by increased carbon dioxide production, even at rest, is common in patients with obesity. It creates an imbalance between the work demands of the respiratory muscles and the capacity to generate tension, resulting in the perception of increased breathing effort.[5] The oxygen saturation was 96% room air when she first came to the emergency ward. Hypoxia, especially chronic hypoxia, can be a predictor of glucose intolerance. Chronic repetitive hypoxic episodes increase the formation of reactive oxygen species (ROS) and cytokines, suppressing insulin secretion and worsening insulin sensitivity. Reactive oxygen species can contribute to the dysregulation of adipocytokines, thereby increasing insulin resistance. Intermittent hypoxia leads to sympathetic activation, chronic inflammation, and oxidative stress, reducing insulin sensitivity, augmentation of gluconeogenesis, and beta cell dysfunction (decrement of insulin secretion).[14,15]

Arterial blood gases were conducted after she was given oxygen. The results are obtained as follows; pH 7.356, PaCO2 of 30.7 mmHg, PaO2 194.5 mmHg, bicarbonate (HCO3) of 17.4 mmHg, base excess of -6.2 mmol/L (Table 3). Based on OHS criteria, there is daytime hypercapnia (arterial carbon dioxide tension (PaCO2) ⩾45mmHg at sea level) [6]. Arterial blood gas examination showed respiratory acidosis. However, the PaCO2 value does not fulfill the criteria for hypercapnia in OHS. We suspect that taking arterial blood gases after oxygen supplementation alters the patient's PaCO2 value. The bicarbonate value was 17.4 mmHg; this value did not match the OHS predictor (bicarbonate ≥27 mEq/L). Multivariate analysis showed that hypercapnia was associated independently with bicarbonate and oxygen saturation. In addition, HCO3 ≥27 mEq/L had high sensitivity and specificity for identifying OHS patients. A sensitive screening tool for daytime hypercapnia is an elevated bicarbonate level due to metabolic compensation of respiratory acidosis.[16,17] There are weaknesses in blood gas analysis. Blood gas analysis performed after receiving oxygen supplementation may change the compensatory mechanisms of the patient's body.

Cabrera Lacalzada and Díaz-Lobato [18] suggested categorizing OHS into mild, moderate, or severe based on daytime PaCO2, daytime arterial oxygen tension (PaO2), body mass index, and the respiratory disturbance index or apnea/hypopnoea index based on polysomnographic findings (Table 4). The presence of complications can also be taken into account. Complications such as pulmonary hypertension, cor pulmonale, left ventricular failure, polycythemia, or history of intensive care in the hospital occur in severe OHS. We categorized the patient as mild OHS based on the results of arterial blood gas analysis (PaO2 value 194.5 mmHg), but the body mass index in this woman was in the severe OHS category (BMI 55.4 kg/m2). The polysomnographic examination was not performed because it was unavailable in our hospital. The patient has left ventricular failure as comorbidity, so we categorized her as having severe OHS for comorbidity criteria.

The criteria that are often used to assess patients with metabolic syndrome, that is, if three of the five criteria are present, namely central obesity (abdominal circumference ≥ 90 centimeters for Asian men and ≥ 80 centimeters for Asian women), triglycerides ≥ 150 mg/dL, or are on medication for hypertriglyceridemia, high-density lipoprotein cholesterol (HDL) < 40 mg/dL in men and < 50 mg/dL in women or are on medication to increase HDL cholesterol levels, systolic blood pressure ≥ 130 mmHg or diastolic ≥ 85 mmHg or are on medication for hypertension, and fasting blood sugar ≥100 mg/dl or type 2 diabetes mellitus.[19,20] Lipid profile examinations were not conducted on patients, but other criteria, such as body mass index 55.4 kg/m2, being treated for diabetes mellitus and hypertension, met the criteria for metabolic syndrome. The lipid profile examination was not carried out due to limited funds.

Table 3. Arterial Blood Gas Analysis Results

Arterial Blood Gas Analysis	Results	Normal Value
pH	7.356	7.35-7.45
PaCO2	30.7	35-45 mmHg
PaO2	194.5	83-108 mmHg
HCO3	17.4	21-28 mmol/L
BE	-6.2	-2.0 - +3.0 mmol/L
AaDO2	31.5	
SO2	99.6%	94 - 99%
Lactate	1.7	0.7 – 2.5 mmol/L

Extensive cohort studies in the general population have demonstrated an increased mortality risk in individuals with overweight and obesity. Patients with obesity, depending on the degree, distribution, and duration of obesity, are at increased risk of developing cardiovascular disease.[21] Patients with severe obesity hypoventilation syndrome are at increased risk of systemic hypertension, diabetes, metabolic syndrome, left ventricular hypertrophy with diastolic dysfunction, pulmonary hypertension, and hepatic dysfunction.[22,23] The results of blood pressure checks during hospitalization showed that the patient met the criteria for grade 1 hypertension (Figure 1). American Heart Association and American College of Cardiology published new guidelines for hypertension management and defined high hypertension as blood pressure at or above 130/80 mmHg. Stage 2 hypertension is blood pressure at or above 140/90 mmHg.[22]

Table 4. Factors Influencing Severity of Obesity Hypoventilation Syndrome: A Proposal For Classification Based on Functional Parameters

	Mild	Moderate	Severe
$PaCO_2$ (mmHg)	46-60	60-80	≥80
PaO_2 (mmHg)	≥70	60-70	≤60
BMI (kg/m^2)	30-40	40-50	≥50
Apnoea/hypopnoea index (event.h^{-1})	<5	5-15	>15
Complications or comorbidities	No	No	Yes

The prevalence of hypertension in patients with OHS is very high, ranging between 55% and 88% (Masa et al., 2018). A study by Alawami et al. found that poor echocardiography views were reported in 33 patients (84.6%) out of 39 patients who had an echocardiogram. LV systolic dysfunction was found in eight patients (24%), and diastolic dysfunction was reported in 18 (60%) out of 30 patients in whom it could be assessed. There was right ventricular (RV) dysfunction in 13 patients out of 25 with good RV views on echocardiogram. Also, from Alawami et al. 16 patients (34%) documented evidence of recurrent atrial or ventricular arrhythmias either during admission to the hospital or after being diagnosed with OHS.[24] The patient's electrocardiogram showed abnormalities with left ventricular hypertrophy, occasional premature ventricular complex, and prolonged QT interval. The echocardiography showed LV systolic dysfunction. The results of a chest x-ray photo with cardiomegaly plus an increase in broncho vascular pattern (Figure 2).

The patient received carvedilol 6.25 mg once daily as an antihypertensive drug. Beta blocker therapy is appropriate in patients with NYHA class II or class III symptoms resulting from left ventricular systolic dysfunction. Carvedilol is the only agent labeled by the FDA for use in patients with heart failure. Patients in the carvedilol group felt better and were less likely to have a severe adverse event related to HF. Carvedilol was the choice of beta blocker for patients with hypertension, hypercholesterolemia, diabetes melitus, and peripheral arterial disease.[24,25]

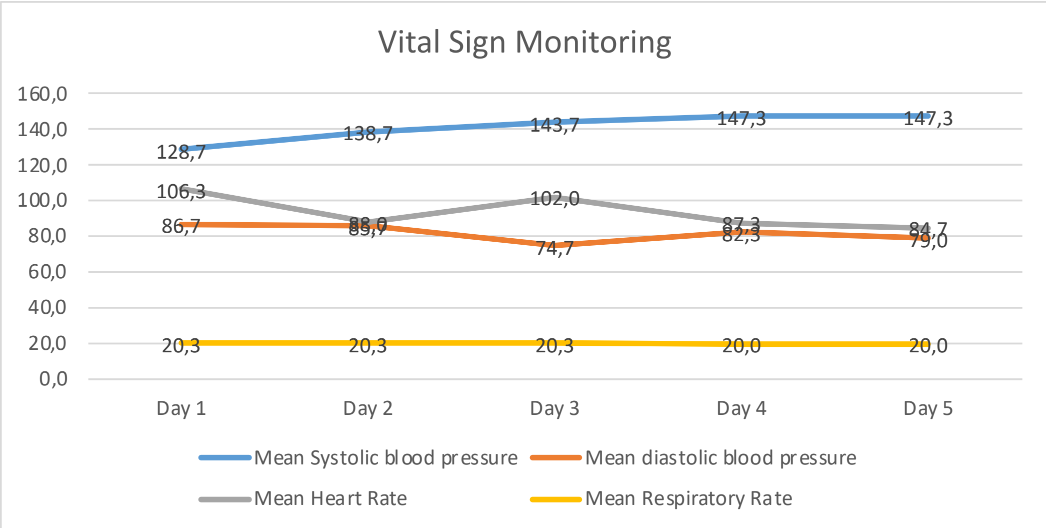

Figure 1. Vital Sign Monitoring

Diabetes is an independent predictor of mortality in OHS. Obesity hypoventilation syndrome should be treated as a systemic disease with respiratory, metabolic, and cardiovascular components that require a multi-model therapeutic approach.[23] In Macavei et al. study, diabetes prevalence was 17.7% (93/525) in the study population, and 60.3% (317/525) had a family history of snoring or sleep apnea. According to Cignarelli et al., sleep-breathing disorders may influence glucose and HbA1c levels independent of central Obesity.[26] In another study, the odds of OHS were 50% higher in those with diabetes mellitus. As measured by elevated HbA1c levels, extended hyperglycemia is associated with an increased basal metabolic rate in OHS via mechanisms of increased gluconeogenesis and lipid oxidation. A high resting metabolic rate had a significant relation with abnormal levels of HbA1c but not with high fasting glucose levels, indicating more of a long-term effect of poor glucose control than short-term effects.[24,26,27]

Based on the results of blood glucose and HbA1C tests, the patient has been diagnosed with type 2 diabetes mellitus. We monitored daily blood glucose and obtained the results in Table 5. Our doctor increased the insulin dose gradually to achieve optimal blood sugar control. Giving oral antidiabetic drugs is not chosen for patients. Internists choose blood sugar control using insulin management. Other co-morbidities suffered are reasons for using insulin. Besides that, the patient has also received education on insulin as a proper control measure to improve blood sugar levels, and the patient has approved it. In the circumstances requiring relatively fast and precise blood sugar regulation, insulin is the best choice because it acts quickly, and the dose can be adjusted according to the results of blood glucose levels. The principle of insulin therapy is to start from a small dose which is increased gradually to prevent hypoglycemia.[28,29] The step of administering insulin therapy to this patient was started with a dose of four units of insulin, followed by eight units of insulin on the second day, sixteen units of insulin on the third day, twenty units of insulin on the fourth day, and twenty-two units of insulin on the fifth day. Insulin therapy was continued after the patient was discharged from the hospital.

Figure 2. Chest X-Ray AP Position with Increased Broncho Vascular Pattern and Cardiomegaly

Table 5. Result of Daily Monitoring Blood Glucose

Treatment Day	Post Prandial Blood Glucose	Dose of Rapid Action Insulin
Day 1	351	4 units
Day 2	307	8 units
Day 3	236	16 units
Day 4	279	20 units
Day 5	226	22 units

Progress during treatment showed positive results, hypoxia improved, and the patient no longer used oxygen supplementation. The patient's blood sugar and blood pressure began to be controlled after taking medicine during hospitalized. She was discharged and continued antihypertensive medication and insulin therapy with an outpatient dose adjustment. The patient is advised to change her lifestyle, lose weight and increase her consumption of vegetables and fruit. The patient was asked to return for control one week later.

CONCLUSION

We present a case of obesity hypoventilation syndrome. Obesity and hypoxia are risk factors for worsening complications in patients with OHS. Handling obesity-related health problems such as hypertension and diabetes mellitus can improve the patient's condition more quickly with better outcomes. Patient education is also essential to prevent worsening of the patient's condition. Correct diagnosis and good management can improve the patient's quality of life and reduce the risk of comorbidities such as heart failure, coronary artery disease, and cor pulmonale. In addition, it can reduce the cost and time of hospital care.

AUTHORS' CONTRIBUTIONS

Made Oka Heryana and Heru Widjono collected research data and wrote this journal. All authors have read and approved the final version of the journal.

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DATA AVAILABILITY STATEMENT

The utilized data to contribute in this journal are available from the author on reasonable request.

DISCLOSURE STATEMENT

The views and opinions expressed in this journal are those of the authors after reviewing various literatures and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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