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# The Metabolic Syndrome and its Correlations with the Obstructive Sleep Apnea Syndrome

KEYWORDS


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|---|---|
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**ABSTRACT** *INTRODUCTION: Obstructive sleep apnea syndrome (OSAS) is a disease mostly occurring in men. It is characterized by breathing pauses during sleep, with intermittent hypoxemia, abnormal sleep, and serious metabolic disorders. The study aims to highlight whether the metabolic syndrome is associated with OSAS.*

*MATERIAL AND METHOD: The population was represented by patients with metabolic syndrome (MS) and OSAS. The following were performed: ENT examination, metabolic exploration: triglycerides (TG), total cholesterol, HDL-cholesterol, a jeun. glycemia and polysomnography.*

*RESULTS: The average age was 47.09 ± 12.94., sex distribution: 34.29% women and 64.71% men. Patients were divided according to the apnea-hypopnea index (AHI) in 2 groups. The metabolic syndrome components showed significant statistical changes in the OSAS group compared to the non-OSAS group, p = 0.0367.*

*CONCLUSIONS: OSAS is associated with the metabolic syndrome and its components. There is a complexity of factors which interfere with the association between OSAS and MS.*

## INTRODUCTION

Sleep respiratory disorders have serious consequences on morbidity and mortality, especially in cardiovascular multifactorial risk. Obstructive sleep apnea syndrome (OSAS) is a common disease characterized by repetitive breathing pauses during sleep, with intermittent hypoxemia, abnormal sleep, and serious neurologic and metabolic disorders. In OSAS, the respiratory pause is the result of total or partial collapse of the upper airway. The respiratory pause is accompanied by bradycardia and increased vagal tone. In resumption of respiration, a micro-awakening occurs, with sympathetic activation and tachycardia. Initially, increased cardiovascular risk has been attributed to obesity associated with obstructive sleep apnea syndrome. However, recent data suggest that OSAS may be independently associated with a series of cardiovascular risk factors such as hypertension, resistance to insulin, impaired glucose tolerance, and dyslipidemia.

There are also several studies in specialized literature which have tried to emphasize complete association of OSAS with the metabolic syndrome, which in turn is a combination of cardiovascular risk factors. It has been shown that sleep deprivation increases the sympathetic tone, alters the appetite control and sensitivity to insulin. In contemporary society, chronic sleep deprivation and easily accessible food sources can alter the appetite regulators hormones and induce obesity. People with a short duration of sleep have low leptin levels and increased ghrelin. These ghrelin, leptin level differences, determine appetite increases, explaining increased body mass index (BMI) observed within sleep deprivation. [1]. The clinical study aims to highlight how common the metabolic syndrome is associated with OSAS, and its components.

## MATERIAL AND METHOD:

The aim of the study is to assess the prevalence of the metabolic syndrome and its components in a group of patients with OSAS compared with patients without OSAS. Another aim is to study the correlation between the metabolic syndrome components and certain clinical characteristics of patients with OSAS. The retrospective study was conducted in May 2010 - July 2011, at the Galenus Medical Center and the Endocrinology Clinic in Tirgu Mures. The study population was represented by 114 patients who were addressed for the metabolic syndrome diagnosis (MS) or OSAS. From the study were excluded patients who had acute infectious diseases or endocrine diseases that might interfere with the lipid metabolism. Clinical and paraclinical examinations have been carried out to all study participants. The patient's data were: anamnesis (smoking, alcohol consumption, urban or rural area of origin, history of metabolic syndrome components, medication administered chronically) weight, height, abdominal diameter measurement, calculating the body mass index (BMI), blood pressure measurement.

Metabolic evaluation included paraclinical evaluation of the defining features for the metabolic syndrome: triglycerides (TG), total cholesterol, HDL-cholesterol, a jeun. glycemia. The triglyceride / HDL-cholesterol ratio was calculated to estimate insulin resistance in patients, having as a model the *Relationship between serum Lipoprotein Ratios and Insulin Resistance in Obesity* [11] study. This demonstrated that the TG / HDL-cholesterol ratio is positively correlated with insulin resistance in obese subjects without diabetes. All patients evaluated for OSAS accused daytime somnolence or at least two of the following conditions: concentration disorders, poor sleep with negative impact on daily activities, whether social or professional, episodes of sleep apnea related to the environment, restless sleep, irritability, snoring.

For OSAS diagnosis, the Epworth daytime sleepiness questionnaire was performed. Patients who had> 12 points score were considered highly susceptible to OSAS and polysomnography was performed using the SLEEPscreen ™ plus portable device and the Domino software analysis. Polysomnography was recorded at night, under physiological sleep, non-medicinal induced, for a period of 6 hours. Polysomnography was performed in willing patients with a <12 Epworth

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score. The OSAS diagnosis was detained for > 5 AHI. Patients who were not subjected to polysomnography and had a <12 Epworth score or who had a <5 AHI were considered without OSAS. Statistical analysis data was performed using the GraphPad application and Excel 2007. Gross descriptive statistical parameters were calculated for all variables.

**RESULTS:**
Of the 114 patients, the data of 62 patients were analyzed, and the demographic characteristics of the entire study sample are presented in Table 1.

**Table 1 -OSAS demographic results versus non-OSAS**

| | OSAS N = 34 | non-OSAS N = 28 | Difference[c] (IC 95%) | P |
|---|---|---|---|---|
| Agea (years)[3] | 45.88 ± 11.48 | 48.57 ± 14.6 | 2.69 (-3.94, 9.31) | 0.4201, NSS |
| Women %, (n)[b] | 34.29% (12) | 25% (7) | | |
| Men %, (n)[b] | 64.71% (22) | 75% (21) | | 0.4201, NSS OR= 0.6111, IC 95% (0.202- 1.85) |
| Epworth[a] score | 9.85 ±4.77 | 4.07 ± 2.46 | -5.78 (-7.77, -3.78) | 0.0001, SS |
| BMI (kg/m$^2$)[a] | 33.75 ±5.32 | 30.86 ±5.27 | -2.88 (-0.17, -5.59) | 0.0367, SS |
| Abdominal diameter (cm) | 115.53± 20.11 | 101.59 ±11.87 | -13.94 (-22.71, 5.39) | 0.0020, SS |
| Smoking: %, (n)[b] | 41.18%, (14) | 26.43%, (13) | 1 | 0.7981, NSS |
| Alcohol: %, (n)[b] | 23.53%, (8) | 39.28%,(11) | 3 | 0.2685, NSS |
| AHI | 53.28± 26.7 (7.6-101.7) | 2.26 ±1.19 (0- 4.6) | | |

[a]Average ± standard devoation [b]Number

NSS- statistically insignificant, SS- statistically significant

To 34 of the 62 patients the OSAS diagnose was present. The remaining 28 patients had an apnea index - hypopnea below 5 per hour of sleep, or an Epworth score with less than 12 points and the absence of specific symptoms of OSAS. In these patients obstructive sleep apnea syndrome was excluded. The number of subjects who had hypertension was statistically significantly higher in the OSAS group. Both glucose and the TG / HDL-cholesterol ratio were higher in the OSAS group. The statistical significance was more important for the TG / HDL-cholesterol ratio, the corresponding value of p being lower than that for glycemia. HDL-cholesterol was lower in the OSAS group than in the non-OSAS group. We did not analyze total cholesterol and LDL values because they do not enter into the definition of the criteria that we used for MS. Triglyceride concentration was higher in subjects with OSAS. The metabolic syndrome was also about two times more frequent in the OSAS group compared to the non-OSAS group (Table 2)

**Table 2. – Metabolic syndrome components**

| | OSAS N = 34 | non- OSAS N = 28 | Difference [c] (IC 95%) | P |
|---|---|---|---|---|
| | | | | |
| HTA n (%) | 23 (67.64%) | 11(39.28%) | | 0.0481, SS |
| Glycemia (mg/dl)[a] | 107.13 ±23.42 | 95.2 ±18.38 | -11.93 (-22.8, -1.05) | 0.0321, SS |
| HDL~ cholesterol[b] (mg/dl)[a] | 45.17 ±13.76 | 52.15 ±10.49 | 6.97 (0.64,13.30) | 0.0314, SS |
| Triglycerides (mg/dl)[3] | 198.41 ± 89.74 | 152.07 ± 62.43 | -46.39(-86.49,-6.27) | 0.0244, SS |
| TG/HDL-col | 4.45 ± 1.51 | 3.04 ± 1.39 | -1.48 (2.15, -0.66) | 0.0004, SS |
| Metabolic syndrome n (%) | 27 (79.41%) | 12 (42.86%) | -15 | 0.0040, SS |

[a]Average ± standard deviation [b] HDL < 40 mg/di, men; <50 mg/dl, women [c]non OSAS column minus OSAS column

In order to describe the relationship between OSAS and obesity, we performed the regression correlation analysis. We considered as dependent variable OSAS, represented quantitatively by the AHI, and as predictor or independent, obesity, represented quantitatively by the body mass index (BMI). We obtained a correlation coefficient R = 0.4647, ranging between (0.25 - 0.5), which means that there is an acceptable degree of association between OSAS and obesity. The relation between the two variables is linear. The determination coefficient R2 = 0.2159, p = 0.0056, statistically significant, expresses the intensity of the linear relationship between the two variables. This means that 21.59% of the OSAS variation may be explained by the linear relationship with obesity. The dispersion diagram (Figure 1) has an increasing trend. Dependence between OSAS and obesity is positive: an increase in obesity involves an increase in OSAS.

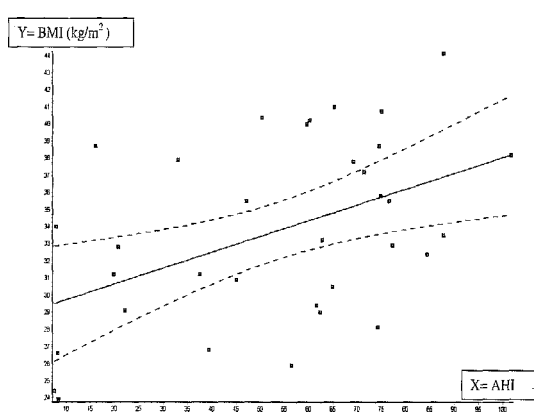


**Figure 1 – The dispersion diagram between AHF and BMI. The continuous line represents linear regression, and the interrupted line represents the confidence interval {CI 95%).**

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Of the 34 patients with OSAS: 4 (11.76%) were diagnosed with mild OSAS (AHI 5-15), 2 females and 2 males; 4 (11.76%) with medium OSAS (AHI 15-30), 1 female , 3 male; 26 (76.47%) with severe OSAS, (AHI> 30), 9 women, 17 men. In patients with OSAS, the abdominal diameter correlated better with AHI than with BMI (R = 0.5476, IC 95% 0.26 - 0.75, R2 = 0.2998) - moderate to good correlation. There is a weak negative correlation between HDL-AHI (R = - 0.1985). Serum triglycerides were poorly correlated with AHI (R = 0.1431), and HTA acceptably correlated with OSAS severity (R = 0.3946) (Table 3)

**Table 3 – R correlation coefficient values for AHI associations with the metabolic syndrome components**

| | | R | IC 95% | coffee | p(ANOVA) |
|---|---|---|---|---|---|
| AH | I –BMI | 0.4647 | 0.15-0.66 | 0.2159 | 0.0056, SS |
| AH | I-Abdominal diameter | 0, 5476 | 0.26 - 0.75 | 0.2998 | 0.0008, SS |
| AHI | -TG | 0.1431 | -0.20-0.46 | 0.0204 | 0.4193, NSS |
| AHI | - HTA | 0.3946 | 0.06 - 0.64 | 0.1557 | 0.0209, SS |
| AHI | - HDl cholesterol | -0.1985 | -0.50-0.15 | 0.0394 | 0.2604, NSS |
| AHI | - TG/HDL-col | 0.2854 | -0.05 - 0.86 | 0.0814 | 0.1018, NSS |
| AH! | - glycemia | 0.4359 | 0.11-0.67 | 0.19 | 0.01, SS |

SS- statistically significant, NSS- statistically insignificant, $R^2$-determination coefficient

**DISCUSSIONS:**

Pathogenesis of cardiovascular disease in the OSAS is not yet fully understood. It appears to be multifactorial and involves several mechanisms such as hyperactivity of the sympathetic vegetative system, selective activation of inflammatory molecular pathways, endothelial dysfunction, abnormal coagulation and metabolic regulation alteration; in the latter is involved insulin resistance and dyslipidemia [2]. Previous studies have shown that OSAS is independently associated with cardiovascular risk factors such as hypertension, insulin resistance, low glucose tolerance and dyslipidemia or with a combination of all these factors as a metabolic syndrome [2,3]. In this study we tried to demonstrate that OSAS is associated with a higher HTA frequency, with HDL- low cholesterol, with greater insulin resistance, with a jeun glycemia and high triglyceride levels and a higher prevalence of the metabolic syndrome.

Unlike the literature data [4], where the male is considered a risk factor for OSAS, in our study it was not a risk factor, although there was a more frequent tendency association with OSAS (OR = 0.6111). The weight of OSAS patients was higher than in the non-OSAS, but the association relation is not very strong, but acceptable (correlation coefficient R = 0.4647). As other studies have shown, we demonstrated that the abdominal diameter may be a good predictor of OSAS, the correlation between OSAS and the abdominal diameter was moderate to good (correlation coefficient R = 0, 5476). However, higher abdominal diameter in the OSAS group may be due to the higher prevalence of MS in this group and a higher BMI in this group. MS prevalence was double in the OSAS group compared to the non-OSAS, p = 0.0040, statistically significant difference. Similar data have been obtained in other studies, what differs is that the OSAS is not associated with insulin resistance [5], or results are contradictory [6]. From this point of view, our study succeeds to estimate insulin resistance by the triglyceride / HDL-cholesterol levels ratio, and not by plasma insulin dosing as in other studies [7].

Analyzing the association of OSAS with each of the metabolic syndrome components, we demonstrated that each of them was more frequent in the OSAS group. There are several studies that say that OSAS is a risk factor for hypertension [2, 8, 9]. The role of intermittent hypoxia in the HTA pathogenesis is still unclear. A causal relationship between intermittent hypoxia during sleep, HTA and cardiac hypertrophy was demonstrated in experimental studies. Other randomized controlled studies have demonstrated reduction of blood pressure after CPAP treatment [2]. Thus the role of OSAS in the HTA pathogenesis can be considered proven. Triglyceride concentration was higher in the OSAS group, and HDL-cholesterol value was lower, as in other previous studies [5]. Altered lipid metabolism and hepatic steatosis associated with OSAS have recently been studied. Total cholesterol value tends to diminish after CPAP treatment.

Further on, HDL-cholesterol protective function is also effective in patients with OSAS [2]. In other studies HDL-cholesterol average increased after OSAS treatment and correlated with decreased AHI, suggesting reversibility of dyslipidemia associated with OSAS [2,10]. There are several reasons due to which OSAS may be independently associated with increased risk factors that define the MS. It is possible that OSAS directly induce growth of these factors, or that OSAS and MS share a common factor such as obesity or a sedentary lifestyle [3]. OSAS may be associated with MS only due to HTA or insulin resistance, which are common to both syndromes. However, the independent association of these components of the metabolic syndrome suggests that this assumption is false. The independent relationships we have demonstrated could give a clear explanation of the reported increased cardiovascular mortality in subjects with OSAS.

**CONCLUSIONS:**

Obstructive sleep apnea syndrome is associated with the metabolic syndrome and with each of its components: increased abdominal diameter, hypertension, low HDL-cholesterol, high triglycerides, low blood sugar, and insulin resistance. MS treatment strategies should include the treatment of OSAS. This study managed to demonstrate that obstructive sleep apnea syndrome is frequently associated with the metabolic syndrome. Through this study I want to highlight the complexity of factors that interfere in the association between OSAS and MS and the interest which should be paid to the examination and diagnosis of OSAS in patients with MS, and conversely, to MS in patients with OSAS. By correct treatment of the two syndromes it can be reduced and prevented associated cardiovascular morbidity, by reducing the risk factors such as dyslipidemia, hypertension, hyperglycemia and diabetes and improve the quality of life in these patients.

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