Metabolic Features In Patients with Obstructive Sleep Apnea Hypopnea Syndrome

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Obstructive sleep apnea hypopnea syndrome (OSAHS) is characterized by repeated breathing pauses during sleep, with slee disruption, intermittent hypoxia, and cardiac, metabolic and neuropsychological disturbances. Metabolic syndrome (MS) is an association of cardiovascular risk factors centered on insulin resistance.The study objective is to calculate the prevalence of MS and its components in a large group of OSAHS patients. We evaluated 350 patients addressed to The Military Hospital Iasi between 2016 and 2017 from the clinical, metabolic and polygraphic poins of view. In 235 of the 350 de patients we found OSAHS. Of the 235 patients with OSAHS, 140 (60%) meet the criteria for MS, versus 29% of the group withut OSAHS (OR = 3.608, CI = 2.1787 - 5.975). Patients with OSAHS were older, more obese, more sedentary, sleepier and presented higher cholesterol values both total cholesterol and HDL fraction, higher trygliceride values, higher blood sugar values and blood pressure values than patients without OSAHS. The prevalence of the MS in OSAHS patients is 60%, similar to what whas reported and higher by 31% than in the non OSAHS group. Certain components and associated conditions are characteristically linked to OSAHS.

Keywords: metabolic syndrome, obstructive sleep apnea, trygliceride, cholesterol

Obstructive sleep apnea hypopnea syndrome (OSAHS) is a condition characterized by repetead breathing pauses exceeding 10 seconds during sleep, caused by dynamic narrowing of the upper airways, with repetitive hypoxaemic episodes and sleep fragmentation, leading to sleep disturbance, daytime somnolence, and severe cario-metabolic complications. OSAHS is characterized by more than 5 breathing pauses (apneas) or reduction or significant reduction (hypopneas) of the airflow per hour of sleep, associated with suggestive symptoms (such as daytime sleepiness). The confirmation of this condition requires polygrapic monitoring during sleep, including monitors for respiratory flow, oxygen saturation, pulse, respiratory movements and if available neurological activity motitoring [1].

Of all the sleep disturbed breathing conditions, OSAHS is mostly associated with the Metabolic Syndrome (MS), beeing part of the association of cardiovascular and metabolic risk factors surrounding insulin resistance. The data regardig the correlation between OSAHS – MS referred to some clinical and laboratory findings (abdominal fat, hypertension, blood lypids, dyabetes) linking the two conditions. There are few data on large databases using homogenous selection criteria[2].

To calculate the prevalence of MS and its components in a large group of patients with SAHOS , comparatively with a group without SAHOS, addressed to the same sleep center.

Experimental part

In a prospective, observational study conducted during 2 years we included 350 patients adressed to the Military Hospital Iasi during 2016 -2017. Clinical, metabolic, and polygraphy werre performed. The inclusion criteria for MS are in the table I.

The diagnostic workup included clinical assessment and nocturnal polygraphy (Porti 7, Germany). OSAHS was established in the presence of more than 5 respiratory

Category	Values
Normal	70 – 100 mg/dL
IFG (impaired fasting glucose):	100 – 125 mg/dL
IGT (impaired glucose tolerance):	140 -180 mg/dL 2 h after glucose intake
Diabetes	Glycemia "à jeun" > 126 mg/dL Or 180 mg/dL at 2h Or any value >200mg/dL

Table 1
DIAGNOSTIC CRITERIA FOR IMPAIRED GLYCEMIA (IDF 2004) [3]

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events (AHI apnea-hypopnea index) followed by significant oxygen desaturation, in symptomatic patients.

The severity of OSAHS :

-Mild OSAHS: AHI 5 -15/h

-Moderate OSAHS: AHI 25 -30/h

-Severe OSAHS: >30/h

Somnolence was assessed using 24 points Epworth scale, using the 24-point scale score, a sleepiness scale score more than 8 being considered a limit normal value and 10 points score a pathological one.

Daily physical effort had been evaluated using a belt pedometer (Kasper- Richter, Germany) carried for a week from initial evaluation, at 3 months , 6 months and one year.

Statistical analysis has been done using SPSS and Excel. The informed consent was obtained from all the patients included in the study.

Results and discussions

The main age in the 350 patients was 52.3 ± 11.9 years. There were 60 women and 290 men.

In 235 of the 350 de patients we found OSAHS, 22 women and 213 men, with mean age 53.1 ± 8.4, mean apnea hypopnea index (AHI) 40.6 ± 23.9/h, mean somnolence index 16.2 ± 5.Epworth, mean Body mass index (BMI) 33.1± 5.47kg/m^2, mean neck circumference 44.6 ± 2.75 cm, mean abdominal circumference 115 ± 12.5 cm.

Of the 235 patients with OSAS:

-40 had mild OSAHS (AHI 9.15 ± 3.16/h); 4 women , 36 men

-48 had moderate OSAHS, (AHI 21.8 ± 4.5/h); 8 women, 40 men

-147 had severe OSAHS (AHI 55.4 ± 17.1/h), 10 women, 137 men

Patients without OSAHS:

-110 patients did not meet the criteria for OSAHS

-43 women, 67 men

-Mean age 49.3 ±17.2 yrs

-Mean BMI 27.9 ± 3.8 kg/ m2

-Somnolence Epworth 8.82 ± 4.1

-Neck 41.9 ± 1.3 cm

-Abdominal circumference 99.8 ± 6.7 cm

Although they do not meet the criteria for OSAHS, these patients cannot be called *heathy*, because they have been adressed because of certain conditions (obesity, snoring, sleep related complaints).

Comparison between parameters of patients with and without OSAHS

Patients with OSAHS were older, more obese, more sedentary, sleepier and presented higher cholesterol values both total cholesterol and HDL fraction, higher tryglicerides values, higher blood sugar values and blood pressure values than patients without OSAHS (table 2).

	N	Min	Max	Medie	DS
Age OSAHS	235	28.00	76.00	53.19	8.39
Age non OSAHS	100	18.00	82.00	49.29	17.42
BMI OSAHS	235	24.00	52.00	33.1234	5.47
BMI non OSAHS	100	21.00	34.00	27.8800	3.385
Somnolence OSAHS	235	4.00	24.00	16.1915	5.09
Somnolence non OSAHS	100	3.00	18.00	8.8200	4.08
Steps OSAHS	98	100.00	7100.00	2777.09	1597.26
Steps non OSAHS	100	550.00	10000	3386.20	2309.99
Neck circumference OSAHS	235	38.00	56.00	44.6170	2.73
Neck circumference non OSAHS	100	40.00	45.00	41.9600	1.30
Abdominal circumference OSAHS	235	89.00	145.00	114.914	12.49
Abdominal circumference non OSAHS	100	91.00	114.00	99.83	6.67
Systolic blood pressure OSAHS	235	120.00	220.00	162.83	23.32
Diastolic blood pressure OSAHS	234	10.00	130.00	92.1581	11.83
Systolic blood pressure non OSAHS	100	100.00	200.00	148.35	20.15
Diastolic blood pressure nonOSAHS	100	60.00	110.00	87.1000	9.72
Cholesterole OSAHS	235	124.00	350.00	226.7	48.92
Cholesterole non OSAHS	86	160.00	369.00	241.267	41.72
LDL OSAHS	229	86.00	190.00	127.13	20.28
LDL non OSAHS	95	98.00	190.00	128.37	16.48
HDL OSAHS	213	11.00	62.00	33.95	9.59
HDL non OSAHS	100	27.00	55.00	42.02	5.51
Triglycerides (TG) OSAHS	163	90.00	600.00	192.06	81.33
Triglycerides (TG) non OSAHS	100	110.00	440.00	162.98	60.368
Glycemia OSAHS	213	77.00	400.00	117.26	44.79
Glycemia non OSAHS	100	79.00	300.00	110.98	32.89
IAH	235	5.00	93.00	40.59	23.85

Table 2
DESCRIPTIVE STATISTIC OF STUDIED CLINICAL AND METABOLIC PARAMETERS IN PATIENTS GROUPS WITH AND WITHOUT OSAHS

Parameters/tests	ANOVA	t Student	Wilcoxon
Age	P= 0.011 (S)	p = 0.03 (S)	
Abdominal circumference	P= 0.150 (NS)	p = 1.99 (NS)	W = 8706.5. p = 2.538 (NS)
Neck circumference	P = 0.493 (NS)	p = 5.81 (NS)	W = 8869.5. p = 1.171 (NS)
BMI	P = 0.225 (NS)	p = 1.35 (NS)	error
Steps	P = 0.23 (NS)	p = 0.03 (S)	error
Somnolence	P = 0.016 (S)	p = 0.0001 (S)	p<0.005 (S)
Systolic blood pressure	P = 0.340 (NS)	p = 0.17 (NS)	W = 17448. p = 0.2 (NS)
Dyastolic blood pressure		p = 0.3 (NS)	W = 13308. p = 0.4 (NS)
Glycemia (Gl)	P = 0.791 (NS)	p = 0.16 (NS)	W = 14772.5. p = 0.2143 (NS)
Total Cholesterole	P = 0.739 (NS)	p = 1.2 (NS)	error
HDL Cholesterole	P = 0.250 (NS)	p = 0.2 (NS)	error
LDL Cholesterole	P = 0.214 (NS)	p = 9.7 (NS)	error
Tyiglicerides	P = 0.955 (NS)	p = 0.001	W = 14772.5. p <= 0.2143 (NS)

Table 3
RESULTS OF THE COMPARISON TESTS BETWEEN THE TWO GROUPS (WITH AND WITHOUT OSAHS)

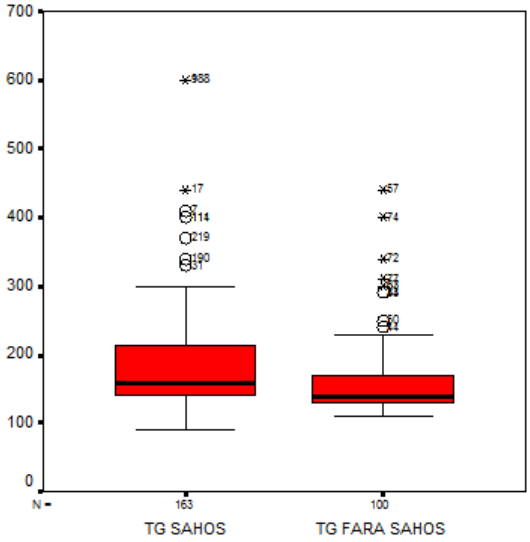

Fig. 1. Serum tryglicerides in patients with and without OSAHS

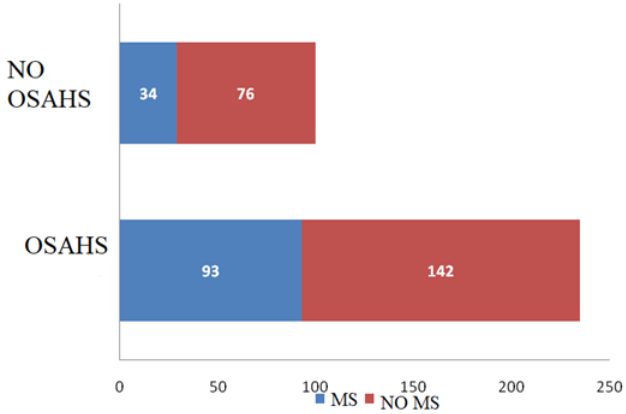

Fig. 2. Patients meeting the ctiteria for MS (IDF, 2004)

One of these comparisons didn't have statistical significance. One explanation might be the abnormal distribution of parameters and also the above observation that patients without OSAHS can't be considered coming from the general population but the carriers of pathological conditions associated with the same symptomatology for which they were sent.

The lack of statistical significance in the comparison between some of these data may be dued to lack of homogeneity in data sets or may be explained by the selection of patients: the majority of the OSAHS patients are severe and the control group belongs to a certain pathology, since they were addressed to a sleep study.

MS and its components

Of the 235 patients with OSAHS, 140 (60%) meet the criteria for MS, versus 29% of the group withut OSAHS (OR AHT= 3.608 , CI = 2.1787 - 5.975).

We can observe a significant percent of patients with severe OSAHS (63%), which corresponds with literature data [4]. In general population, AHT has a prevalence between 29-31%, blood sugar dysfunctions have a prevalence between 14-20%, obesity has a prevalence between 6-26% in Europe and atherogenic dyslipidemia has a high percent prevalence up to 70% in adult population [5-7].

According to literature data MS in adult general population has been estimated between 22 and 39% [8, 9].

Even they do not have all the diagnostic criteria for OSAHS, patients from control group can't be seen as *healthy,* because they have been sent to the sleep lab to be assessed for specific symptoms (snoring, nocturnal dyspnea , sleepiness, abnormal movements in sleep etc).

Lack of statistical signification between differences in values concerning abdominal circumference, throat circumference, BMI, total cholesterol, HDL cholesterol, LDL cholesterol, tryglicerides, systolic blood pressure and dyastolic blood pressure can be dued to lack of data homogeneity in data sets and also to the fact that patients without OSAHS does not belong to general population. Also, even if a high percentage of a certain population has one pathological parameter we cant say that the medium value of this parameter is higher in that population than control group.

A surprising finding was the low value of cholesterol in OSAHS group (18 pacients with total cholesterol value under 150 mg/dL, all having AHI over 44/h).We can take in consideration the hypothesis of a liver syndrome(liver

OSAHS	No OSAHS	Odds Ratio (OR)
140 with MS: 75 m . 18 f* (60%)	**34 with MS**: 28 m. 6 f (29%)	3.6
Abdominal circumference pathologic 230: 22 f. 208 m (98%)	**Abdominal circumference pathologic 93**: 87 m. 6 f (85%)	8.1176 CI 2.86 - 23.01
AHT (arterial hypertension) 182 (77%) Normal high (130- 140) 35 Gr 1 (150-160) 58 Gr 2 (160-180) 49 Gr 3 (>180) 40	**AHT (arterial hypertension) 62** (56%) Normal high (130- 140) 11 Gr 1 (150-160) 22 Gr 2(160-180)15 Gr 3 (>180) 15	2.6981 CI 1.64 - 4.44
HDL abnormal 172; 153 m. 19 f (73%)	**HDL abnormal 65**: 45 m. 20 f (59%)	1.8972. CI 1.2 - 3.1
Hypercholesterolemia: 160 (68%)	**Hypercholesterolemia: 66** (60%)	1.4222 CI 0.9 - 2.3 **NS**
TG pathologic146 (62%)	**TG pathologic 44** (40%)	2.4607 CI 1.52 - 3.9
LDL pathologic 219 (93%)	**LDL pathologic 45** (41%)	19.7 CI 10.33 - 37.55
Gl. control: 148 (63%) IFG: 98. IGT:82 Diabetes: 50	**Gl. control:55** (50%) IFG: 40.IGT: 28 Diabetes:: 15	1.7011 CI 1.06 - 2.73
Impaired body weight: 232 (99%) Overweight: 51 **Obesity: 181** (77%) class I: 111 class II: 47 class III: 6 morbid obesity: 9	**Impaired body weight: 86** (78%) Overweight: 46 **Obesity: 40** (32%) class I: 32 class II: 8	21.812 CI 6.35 - 74.86
Somnolence >8: 216 *Somnolence* >10:**189**	Somnolence > 8: 54 Somnolence >10: **28**	

Table 4
PATIENTS WITH ABNORMAL VALUES OF SOME CARDIO-METABOLIC PARAMETERS

congestion/alcohol consumption/hipoxemia). Analysing medical files of these pacients we identified liver pathology in all 18 patients.

MS is a prediabetic condition which brings together different independent metabolic alterations with high cardiovascular risk through initiation and perpetuation of an inflammatory and degenerative atherosclerotic vascular process, in which insulinoresistance and compensatory hyperinsulinemia represent the main pathogenic element. Epidemiological studies of prevalence done on different group populations showed that MS is a major cardiovascular risk factor and also a diabetes mellitus risk factor [10,11].

MS represents a high risk for the birth of a wide spectrum of diseases. The most extensive studies being on cardio-metabolic risk of diabetes. Every component of element MS is in fact, a factor that can determin a high cardiovascular risk but also it is important to discuss the aggregate cardiovascular risk in these patients. More than that , elements of MS that are not found in definition criteria (proinflammatory status, prothrombotic status, insulin resistance) generate cardiovascular risk.

The association of visceral fat, systemic inflamation, hyperinsulinism and atherogenic dyslipidemia makes OSAHS to be considered nowadays as a systemic disease, one of the manifestation of *metabolic syndrome* and not only a local anomaly of upper airways [12].

Pathogenic and epidemiological links between OSAHS and MS are so tight that we can define nowadays a new concept which includes atherogenic dyslipidemia, insulin resistence, blood pressure, excessive abdominal fat and OSAHS: Z metabolic syndrome [13-16].

Metabolic syndrome is controversial as an independent clinical entity being considered more as a constelation of risk factors, (a working pattern) which includes a series of criteria that, by reuniting, define a category of patients.

Its prevalence differs widely with age, studied population and diagnostic criteria. A french study done on a male group shows a prevalence of MS of 5% at 30 years of age untill 17.5% over 64 years old. In North America, this prevalence gets to 50% in males over 50 years old. The differences in prevalence according to the 3 diagnostic criteria (OMS, NCEP-ATP III and IDF) are between 10 - 15%.

The four main elements of MS (excessive abdomminal fat, hypertension, insulin resistance and dyslipidemia) are grouped together in order to emphasize and define the management of obesity risks so that for a clinician to become obvious the approach no matter the pattern defined.

Experts reccomand as management strategy to change the lifestyle, antihypertensive molecules like sartans,

lipemiants and metformin but they emphasize diet and exercise.

In patients with OSAHS, MS can be 9 more times present than in general population [11]. In general population, AHT has a prevalence between 29 - 31% (5-7), blood sugar dysfunctions have a prevalence between 14-20%, obesity has a prevalence between 6-26% in Europe and atherogenic dyslipidemia up to 70% in adult population. According to literature data prevalence of MS in general population has been estimated between 22 and 39% [11].

In patients with OSAHS from our study prevalence of AHT was found to be 77% (close to the one presented in literature for OSAHS of 70%), global prevalence of dyslipidemia was found to be almost 70% (according to literature data), obesity had a prevalence of 99% and metabolic syndrome of 60% (close to the one reported for other population with OSAHS).

Conclusions

The prevalence of the MS in OSAHS patients is 60%, similar to hat whas reported and higher by 31% than in the non OSAHS group. Certain components and associated conditions are characteristically linked to OSAHS.

References

1.GUILLEMIAULT C, FRAMHERZ S. Principles and Practice of Sleep Medicine. Eds Kryger MH, Roth T. & Dement WC. Elsevier Saunders, Philadelphia, 2005, p.780

2.GRUNSTEIN RR. Sleep **19**, 1996, p. S218

3.COLLINS FL, GRUNSTEIN RR, SULLIVAN CE. Thorax. **53,** 1998, p.S25

4.MCNICHOLAS WT, BONSIGNORE MR. Eur Respir J **29**, No. 1, 2007, p. 156

5.BAGUET JP, HAMMER L, LEVY P et al. J Hypertens, **23**,No. 3, 2005, p.521

6.PEPPARD PE, YOUNG T, PALTA M, SKATRUD J. N Engl J Med **342**, 2000, p. 1378

7.LOGAN AG, PERLIKOWSKI SM, MENTE A, et al. J Hypertens **19**, 2001, p. 2271

8.MCLAUGHLIN T, ABBASI F, CHEAL K, CHU J, LAMENDOLA C, REAVEN G. Ann Intern Med. **139**, No.10, 2003, p.802

9.*** NATIONAL HEART, LUNG, AND BLOOD INSTITUTE JOINT NATIONAL COMMITTEE ON PREVENTION, DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE; NATIONAL HIGH BLOOD PRESSURE EDUCATION PROGRAM COORDINATING COMMITTEE. THE SEVENTH REPORT OF THE JOINT NATIONAL COMMITTEE ON PREVENTION, DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE: The JNC 7 Report. JAMA. **289**, 2003, p. 2560

10.OGRETMENOGLU O, SUSLU AE, YUCEL OT, ONERCI TM, SAHIN A. Laryngoscope, **115**, No. 8, 2005, p. 1493

11.VGONTZAS AN, BIXLER EO, CHROUSOS GP. Sleep apnea is a manifestation of the metabolic syndrome. Sleep Med Rev. **9** No.3, 2005,p. 211

12.STROHL KP. Sleep, No.19, 1996, p. 225

13.ODRETMENOĐLU O, SÜSLÜ AE, YUCEL OT, ONERCI TM, SAHIN A. Laryngoscope, **115**, No. 8, 2005, p. 1493

14.ROMERO-CORRAL A, SOMERS VK, SIERRA-JOHNSON J, THOMAS RJ, COLLAZO-CLAVELL ML, KORINEK J, et al. Int J Obes; **32** No. 6, 2008, p. 959

15.REZUS, E., LEON CONSTANTIN,M.M., REZUS,C., Rev. Chim. (Bucharest), **66**, no.7, 2015, p.1015

16.GROZDAN, A.M., GHIURU,R., DUCEAC, L.D., BODESCU,M.M., Rev. Chim..(Bucharest), **67** no. 12, 2016, p.2654

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