



ORIGINAL ARTICLE

Sleep apnoea-hypopnoea syndrome in the obese and non-obese: Clinical, polysomnographical and clinical characteristics^{☆,☆☆}



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Abstract

Introduction: Sleep apnoea-hypopnoea syndrome (SAHS) and childhood obesity are two high prevalence conditions that represent a public health challenge.

Objective: To analyse the association between both and comparing child groups that had or did not have both conditions.

Patients and methods: A prospective study in children (3–14 years), referred to the “Multidisciplinary Sleep Unit” due to suspected SAHS, between 1 November 2015 and 1 August 2017. The following parameters were evaluated: anthropometry, symptoms, blood pressure, ear, nose, and throat examination, polysomnography (nocturnal PSG) and laboratory tests.

Results: A total of 67 children were evaluated (64% non-obese (NOb) and 36% obese (Ob). It was observed that the Ob were older ($P < .001$), slept less hours ($P = .028$), did less physical exercise ($P = .029$), ate less in the school dining room ($P = .009$), had a lower sleep efficiency, and had abnormal values in carbohydrate and lipid metabolism.

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The children with SAHS were younger ($P = .010$), a high percentage of daytime sleepiness ($P = .001$), and breathing through the mouth ($P = .006$), greater percentile of diastolic blood pressure ($P = .019$) and a lower IGF-1 ($P = .003$) than those that did not have SAHS. The comparison of the SAHS NOB and SAHS Ob groups, showed that the first group were younger ($P = .010$), snored more ($P = .012$), had a more severe SAHS (IAH 13.1 vs 5.4, $P = .041$), and a higher GOT ($P < .001$). In the second group, they slept less hours $P = .038$) and showed lower values of glucose ($P = .039$), insulin ($P < .001$), and HOMA ($P < .001$).

Conclusion: The behaviour of SAHS is different in obese children and non-obese children, with differences in age, clinical characteristics, severity of SAHS, and metabolic changes. The children diagnosed with SAHS were in the higher percentile of diastolic blood pressure. Obesity was associated with worse sleep quality, and changes in carbohydrate and lipid metabolism.

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PALABRAS CLAVE

Síndrome de apnea hipopneas del sueño;
Trastornos respiratorios del sueño;
Apnea obstructiva del sueño;
Niño;
Obesidad infantil;
Polisomnografía;
Metabolismo

Síndrome de apneas-hipopneas durante el sueño en obesos y no obesos: características clínicas, polisomnográficas y metabólicas

Resumen

Introducción: El síndrome de apneas-hipopneas del sueño (SAHS) y la obesidad infantil son dos entidades con alta prevalencia que constituyen un problema de salud pública.

Objetivo: Analizar la interacción entre ambas, comparando grupos de niños que presentaban o no ambas condiciones.

Pacientes y metodología: Estudio prospectivo en niños (3–14 años), remitidos a la Unidad Multidisciplinar de Sueño por sospecha de SAHS, entre el 1/11/2015 y el 1/08/2017. Se evaluaron los siguientes parámetros: antropometría, síntomas, tensión arterial, exploración otorrinolaringológica, polisomnografía (PSG nocturna) y estudio analítico.

Resultados: Se valoraron 67 niños, 64% no obesos (NOB) y 36% obesos (Ob).

Se observó que los Ob tenían más edad ($P < .001$), dormían menos horas ($P = .028$), realizaban menos ejercicio físico ($P = .029$), comían menos en comedor escolar ($P = .009$), tenían menor eficiencia del sueño y presentaban valores alterados en el metabolismo hidrocarbonado y lipídico.

Los niños que presentaba SAHS tenían menor edad ($P = .010$), un mayor porcentaje de somnolencia diurna ($P = .001$) y respiración bucal ($P = .006$), mayor percentil de tensión arterial diastólica ($P = .019$) y menor IGF-1 ($P = .003$) que los que no presentaban SAHS.

La comparación de los grupos de SAHS NOB frente SAHS Ob, reveló que los primeros eran de menor edad ($P = .010$), roncaban más ($P = .012$), tenían mayor severidad del SAHS (IAH 13.1 vs 5.4, $P = .041$) y mayor GOT ($P \leq .001$) y en el segundo grupo, se objetivó que dormían menos horas ($P = .038$) y mostraban valores mayores de glucosa ($P = .039$), insulina ($P < .001$) y HOMA ($P < .001$).

Conclusión: El comportamiento del SAHS es diferente en los niños con y sin obesidad, presentando diferencias en la edad, características clínicas, severidad del SAHS y alteraciones metabólicas. Los niños con diagnóstico de SAHS tienen mayor percentil de tensión arterial diastólica. La obesidad conlleva una peor calidad de sueño y alteraciones en el metabolismo hidrocarbonado y lipídico.

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Introduction

Sleep-related breathing disorders are very frequent in the paediatric population and are associated with important repercussions on health, such as changes in growth, metabolic, cardiovascular and neurocognitive disorders and impaired quality of life.

Sleep apnoea-hypopnoea syndrome (SAHS) is the most prevalent sleep-related breathing disorder and affects 2%–4% of children aged 2–6 years, a period that coincides with the peak of physiological adenotonsillar hypertrophy,¹ which is the most frequent cause of paediatric SAHS.

The diagnosis of SAHS is based on clinical suspicion, the history and the findings of the physical examination, and its

confirmation requires performance of a sleep study, respiratory polygraphy or overnight polysomnography (PSG).²

On the other hand, there is an association between obesity and SAHS in adults that is starting to be seen in children with increasing frequency. The NANOS study in children with obesity in Spain found a high prevalence of SAHS that ranged from 21.5% to 39.5%.³

The global prevalence of childhood obesity has reached the proportion of an epidemic and has become a public health problem.⁴ As occurs in the rest of the world, prevalence of obesity in Spain continues to grow, the most recent ALADINO study in children aged 6–9 years identified obesity in 20.4% of boys and 15.8% of girls.⁵

Obesity and SAHS each cause significant morbidity independently. Our aim was to assess the potential interaction between the two, which would be evinced by the presence of clinical, polysomnographic and metabolic differences between obese and non-obese patients with SAHS.

Thus, we conducted a study with the objective of describing the characteristics of children referred to a sleep unit for suspected SAHS. The study was conducted in a cohort of children with and without obesity, allowing us to analyse the differences between several groups: obese (Ob) versus non-obese (NOB), with SAHS versus without SAHS and obese with SAHS (SAHS-Ob) versus obese without SAHS (SAHS-NOB).

Sample and methods

We conducted a prospective study in children of both sexes aged 3–14 years referred for suspected SAHS to the Multidisciplinary Sleep Unit of a tertiary care university hospital after receiving the approval of the Research Ethics Committee. We obtained the informed consent of the parents and/or legal guardians of every participant as well as the assent of all children aged more than 12 years. We assigned a code to each participant to guarantee the anonymity and confidentiality of the data.

The sample was obtained by consecutive enrolment of children referred for clinical suspicion of SAHS (presence of snoring and/or pauses in breathing during sleep) that met the inclusion criteria and did not meet any exclusion criteria. The inclusion criteria were: 1) patients referred from a primary care paediatrician aged 3–14 years; 2) signed informed consent. We excluded children with craniofacial anomalies, dysmorphic syndromes, psychomotor delay or genetic/neuromuscular disorders as well as children with a history of adenotonsillectomy or previous treatment of SAHS and children for whom we did not obtain signed informed consent.

We defined obesity as a body mass index (BMI) at or above the 95th percentile for age and sex (Fundación Orbegozo 2004 growth tables).⁶

We divided the sample in 2 groups based on the presence or absence of obesity: obese group (Ob) and non-obese group (NOB).

The following protocol was implemented in all children: 1) documentation of demographic and clinical characteristics (sex, ethnicity, perinatal history). 2) General medical history and sleep questionnaire: Pediatric Sleep Questionnaire, validated abridged version in Spanish (Chervin questionnaire).⁷ A score of 0.33 or higher was considered

suggestive of SAHS.⁸ 3) Physical examination with documentation of anthropometric measurements: weight (kg), height (m), BMI (kg/m²) and the corresponding percentiles⁶; morning blood pressure (BP) measured with an automatic monitor. Blood pressure was measured 3 times, and the mean of the last 2 measurements was used for the analysis of BP percentiles.⁹ 4) Ear, nose, throat (ENT) examination with assessment of adenoid and tonsillar hypertrophy. Tonsil size was graded on a scale from 0 to IV based on the size and the percentage of the of the lateral dimension of the oropharynx occupied by the tonsils. Grade 0: absence of tonsils; Grade I: tonsils occupy 0%–25% of lateral dimension of oropharynx; Grade II: 25%–50%; Grade III: 50%–75%; Grade IV: 75%–100%.¹⁰ The adenoids were examined by anterior rhinoscopy and with a fibre optic endoscope.

All children underwent a nocturnal laboratory-based PSG in the Multidisciplinary Sleep Unit, which included the use of electroencephalography, electrooculography (both eyes), electromyography (tibialis and submentalis), electrocardiography, monitoring of oronasal air flow through a thermistor channel, plethysmography for monitoring of thoracic and abdominal movements, position sensors to monitor body position, monitoring of oxygen saturation and heart rate by pulse oximetry, monitoring of snoring and air flow through pressure transducer channels in nasal prongs and continuous transcutaneous carbon dioxide (CO₂) monitoring. We applied the criteria published in 2012 by the American Academy of Sleep Medicine (AASM) for scoring of sleep stages and associated events.¹¹ We expressed the relative duration of each sleep stage as the percentage (%) of the total duration of sleep. We defined apnoea index (AI) and the apnoea-hypopnoea index (AHI) as the number of apnoeas and the number of apnoeas and hypopnoeas per hour of sleep, respectively. We also calculated the obstructive AHI (oAHI), central AHI (cAHI) and respiratory disturbance index (number of apnoeas, hypopnoeas and respiratory effort-related arousals [RERAs] per hour of sleep).

In adherence with the criteria established in the national consensus document for SAHS in children,² the diagnosis of SAHS and indication of treatment were based on the AHI being 3 or greater, whether or not obstructive hypopnoea had been detected by PSG.

We performed laboratory tests for inflammatory, metabolic and endocrine markers. Blood samples were collected the morning after the PSG.

Statistical analysis

We used the software SPSS version 22 (Chicago, IL, USA). We have expressed quantitative data as median and interquartile range and categorical data as absolute frequency and percentage distributions in comparison with another dichotomous variable. We compared continuous data using the Mann-Whitney *U* test and categorical data with the chi square test or Fisher exact test. We defined statistical significance as a *P*-value of .05 or less.

Results

Between 1/11/2015 and 1/08/2017, 67 children enrolled in the study, 60% boys and 40% girls, referred for clinical

Table 1 General characteristics of children without versus with obesity and without versus with SAHS.

	Non-obese	Obese	<i>P</i>	No SAHS	SAHS	<i>P</i>
M – F	67% -33%	46%-59%	.084	58%- 42%	61%-39%	.800
Age (range)	5 (3.7-6)	8.5 (6.5-11.5)	<.001	6.7(4.6- 8)	4.8(3.5-6.6)	.010
BW pct (range)	35.5 (16- 78.2)	69 (25-80)	.241	45(23- 78)	37 (18.7- 79.2)	0.778
Tonsil grade						
0	0%	4%	1.000	3%	0%	1.000
I-II	35%	58%	.263	55%	33%	.368
III-IV	65%	38%	.043	42%	67%	.057
Chervin test +	74%	63%	.307	68%	72%	.689
Mouth breathing	72%	38%	.006	42%	75%	.006
Somnolence	19%	8%	.311	0%	28%	.001
Regular snoring	71%	53%	.157	62%	75%	.066
Morning dry mouth	86%	50%	.001	74%	72%	.856
SBP pct (range)	90 (50-95)	90 (50-98)	.538	90 (50- 95)	90 (60-95)	.236
DBP pct (range)	90 (90-95)	90 (50-93.7)	.312	90 (50- 90)	90 (90-95)	.029
Sleep duration, h (range)	10 (10-11)	10 (9.3-10)	.028	10(8-10)	10(10-10.8)	.024
PA, h (range)	7 (3-9)	3 (2-7)	.029	4 (2-8.2)	7 (3-7)	.366
School lunch	49%	17%	.009	39%	36%	.826
Breakfast daily	93%	79%	.124	87%	89%	.000
5 meals/day	91%	75%	.149	81%	89%	.495
Screen time, h (range)	1.3 (1-2)	1.3 (1-2)	.272	1 (1-2)	1.3 (1-2)	.249

AHI, apnoea-hypopnoea index; BW, birth weight; DBP, diastolic blood pressure; F, female; h, hours; M, male; PA, physical activity; pct, percentile; SAHS: sleep apnoea-hypopnoea syndrome; SBP, systolic blood pressure; SAHS, sleep apnoea-hypopnoea syndrome.

suspicion of SAHS to the Multidisciplinary Sleep Unit. The median age was 5.5 years (interquartile range, 4.3–7.7). Most participants were Caucasian (86%), while 13% were Latin American and 2% Asian.

Sixty-four percent of participants (43) were obese, and 36% (24) were not obese. Tonsillar hypertrophy was detected

in 93% of children (grades II-III-IV), snoring in 91% and mouth breathing in 60%.

In this case series, 14 patients had a family history of SAHS (16% in the father, 2% in the mother and 5% in siblings). The findings of the family history of metabolic disorders were: obesity in the father in 28%, the mother in 17% and a sibling

Table 2 Neurophysiological polysomnographic parameters.

Nocturnal PSG	Non-obese	IQR	Obese	IQR	<i>P</i>	No SAHS	IQR	SAHS	IQR	<i>P</i>
Sleep duration, min	514.5	477-540.8	455.8	436.3-520.5	.006	501.5	441-522.6	502.2	454.6-537.5	.481
Sleep efficiency, %	84.5	80.7-89.1	78.1	70.9-85.9	.017	82	76.8-86.3	84.6	77.7-89.5	.285
NREM latency, min	28	16.5-42.5	33.2	16.6-43.3	.633	28	17-44.5	29.7	13.8-42.2	.758
REM latency, min	84.5	66-106	119.7	90.6-156.3	.005	90.5	63.5-120	92.7	74.3-136.7	.517
Intervening wake, %	8.6	7-12.5	13.7	8.15-19.4	.012	11.5	7.3-16.5	8.3	7-15.4	.450
Stage 1, %	9.2	6.4-13.5	7.85	5.5-11.5	.131	8.2	5.2-12	10.2	7.1-13.7	.064
Stage 2, %	31.7	27.3-38	37.1	31.6-45.7	.014	33.5	29.8-44.2	32.9	26.4-3	.237
Stage 3, %	32.6	28.6-36.1	33.1	24.7-36.5	.709	33	26.2-36.7	32.6	29.4-35.7	.870
REM sleep, %	25	21.1-27.2	22.3	18.5-27	.429	24	19.1-26.4	24.5	21.2-29	.436
Arousals, <i>n</i>	116	71-159	79	49.2-102.2	.011	76	49-103	115	75-157.5	.012
Arousal index	13	8.7-20.5	10.5	6.7-12.9	.037	9.2	7.6-12.8	13.1	10.2-20.1	.005

IQR, interquartile range; Lat, latency; min, minutes; PSG, polysomnography; SAHS, sleep apnoea-hypopnoea syndrome; Wake, wakefulness.

Table 3 Respiratory polysomnographic parameters.

Nocturnal PSG	Non-obese	IQR	Obese	IQR	<i>P</i>	No SAHS	IQR	SAHS	IQR	<i>P</i>
Ap. centrales (n)	6	1-14	1.5	0-4.7	.022	1	0-5	7	2.2-14.7	.002
Ap. obstructivas (n)	5	0-23	0	0-5.5	.017	0	0-0	12.5	1-46.2	<.001
Ap. mixtas (n)	0	0-1.0	0	0-0	.159	0	0-0	0	0-2	.001
Hipopneas (n)	11	3-7	9	2-25.7	.206	2	0-5	35	17.7-79.5	<.001
RERAS (n)	22	5-36	21.5	4.2-29.7	.399	7	3-22	29	16.5-50.7	<.001
IAH	4	1.3-14.4	1.8	0.6-5.2	.082	1	0.2-1.5	8.2	4.2-18.4	<.001
IAH REM	4.8	2.3-16.6	2.5	0-8.4	.014	2	0-3.2	10.6	4.4-33.8	<.001
IAH NREM	2.9	0.5-12.8	2	0.3-5.5	.333	0.5	0-0.9	7	3.4-13.5	<.001
IAH supino	7.0	1.5-24.3	3.2	0.6-6.9	.078	0.9	0-1.9	12.1	7-28.4	<.001
IAHo	2.4	0.59-13.2	1.7	0.2-4	.132	0.4	0-1.1	7.6	3.5-15.2	<.001
IAHC	0.6	0.18-1.5	0.17	0-0.6	.015	0.1	0-0.6	0.8	0.3-1.7	.001
R.D.I	7.1	2.3-20.4	4.5	1.80-7.9	.166	1.8	0.8-4.2	12.2	7.7-23.3	<.001
Sat O ₂ m.(%)	97	96.5-97.3	96.6	96.2-97.1	.190	97.1	96.6-97.5	96.7	96.1-97	.012
ODI %	3.9	1.6-8.2	2.3	1.20-6.6	.150	1.6	0.7-2.8	7.2	3.9-10.3	<.001
Pet CO ₂ mmHg	0.5	0-9.2	0	0-3.4	.312	0	0-6	0	0-8.4	.884

AHI, apnoea-hypopnoea index; Ap, apnoea; cAHI, central apnoea-hypopnoea index; NREM AHI, non-REM sleep apnoea-hypopnoea index; oAHI, obstructive apnoea-hypopnoea index; ODI, oxygen desaturation index; PETCO₂, partial pressure of end tidal CO₂; RDI, respiratory disturbance index; REM AHI, REM sleep apnoea-hypopnoea index; RERA, respiratory event-related arousal; SAHS, sleep apnoea-hypopnoea syndrome; SatO₂, oxygen saturation.

in 4% of participants; dyslipidaemia in the father in 16%, the mother in 5% and a sibling in 2% of participants; high BP in the father in 6% and the mother in 5% of participants.

The results of the Chervin questionnaire for detection of sleep disorders were positive in 70% of the patients. Based on the findings of the PSG, 39% of participants had SAHS without

obstructive hypopnoea, 4% SAHS with obstructive hypopnoea and 24% reduced air flow without meeting criteria for SAHS, while 33% did not have respiratory problems.

When it came to management, 39% of patients underwent an adenotonsillectomy and 1% an adenoidectomy, 18% were treated with sleep hygiene and dietary measures,

Table 4 Metabolic parameters in children without vs with obesity and without vs with SAHS.

Laboratory results	Non-obese	IQR	Obese	IQR	P	No SAHS	IQR	SAHS	Rango inter	P
Glucose, mg/dL	81	78-86	86.5	82-91	.003	82	80-89.5	84.5	79-88	.885
Uric acid, mg/dL	4	3.4-4.3	4.1	3.5-4.8	.101	4.3	3.6-4.7	3.6	3.3-4.3	.021
Creatinine, mg/dL	0.3	0.3-0.4	0.5	0.4-0.5	<.001	0.4	0.4-0.5	0.3	0.3-0.4	.024
Phosphorus, mg/dL	5	4.7-5.2	4.8	4.4-5.1	.045	4.9	4.6-5.2	4.9	4.6-5.2	.621
AST, IU/L	27	23.5-30.5	21	17.5-25.7	.001	23	20.5-29.5	26.5	23-30	.169
ALT, IU/L	16	14-19	17	14.2-20	.320	17	14-20	15.5	14-19	.305
TG, mg/dL	48	40-63	69.5	53-86.5	.002	55	44.5-77.5	52	43.5-70	.689
Total cholesterol, mg/dL	156	142-182	157	149.2-175	.899	157	146-177	158.5	141.5-181.2	.929
CPR, mg/dL	0	0-3	1	0.25-2.7	.230	1	0-3	1	0-3	.453
Vitamin D, ng/mL	27.8	19.3-37	24.3	13.8-31.4	.102	26.6	17.4-35.8	25.7	19.3-32.1	.741
Free T4	1.4	1.3-1.5	1.4	1.2-1.4	.365	1.3	1.2-1.4	1.4	1.3-1.6	.016
Ferritin, ng/mL	38	29-45	48	31-61.5	.041	39	30-52.5	40.5	29.7-51.5	.956
IGF-1, ng/mL	86.7	58.7-154	165	129.2-272.7	<.001	161	106.2-227	97.8	59.3-146.5	.003
Insulin, μ U/L	5	3.3-7.6	16.6	12-24.4	<.001	8.2	4.6-15.7	6.3	3.9-14	.393
HOMA	1	0.7-1.5	3.9	2.1-5.3	<.001	1.6	0.93-3.5	1.4	0.7-3	.505

ALT, alanine aminotransferase; AST, aspartate transaminase; CPR, C-reactive protein; HOMA, insulin resistance index; IGF-1, insulin-like growth factor-1; IQR, interquartile range; SAHS, sleep apnoea-hypopnoea syndrome; TG, triglycerides.

5% received pharmacological treatment (nasal steroids and antileukotrienes) and 25 patients remained in follow-up for monitoring of their condition.

Comparison of children with and without obesity

The comparison of children with obesity (Ob, $n = 24$) and children without obesity (NOb, $n = 43$) (Table 1), revealed a significantly younger age, higher prevalence of mouth breathing, higher prevalence of morning dry mouth and greater tonsil size in the NOb group, with no significant differences based on sex, birth weight or score in the Chervin questionnaire.

In the Ob group, 50% of children had obese fathers and 30% obese mothers, compared to 17% of fathers and 10% of mothers in the NOb group ($P = .005$ y $P = .032$).

There were also significant differences in the comparison of sleep hygiene and dietary habits in the Ob and NOb groups (Table 1), as Ob slept fewer hours, exercised fewer hours a week and were less likely to use the school lunch services. The comparison of the nocturnal PSG parameters in the Ob vs NOb groups (Tables 2 and 3) revealed that obese children had a shorter total sleep duration TTS, a lower sleep efficiency, fewer arousals, lower REM AHI and cAHI, a longer REM latency and higher proportions of intervening wakefulness and stage 2 sleep.

When it came to metabolic parameters (Table 4), we found higher levels of glucose, creatinine, triglycerides (TG), basal insulin, ferritin and insulin-like growth factor-1 (IGF-1) levels and a higher homeostatic model assessment (HOMA) index (indicator of insulin resistance) in children with obesity.

Comparison of children with and without SAHS

When we compared children with SAHS ($n = 36$) and without SAHS ($n = 31$) (Table 1), we found that the SAHS group was significantly younger, had a significantly higher prevalence of daytime somnolence and of mouth breathing and had diastolic blood pressures (DBP) at significantly higher percentiles compared to the group without SAHS. We did not find significant differences between these groups in sex distribution, tonsil size or the results of the Chervin questionnaire.

The comparison of sleep hygiene and dietary habits (Table 1), polysomnographic parameters (Tables 2 and 3) and metabolic parameters (Table 4) revealed significant differences between children with and without SAHS groups. Children with SAHS slept more hours at night, had more arousals and a higher arousal index (without significant differences in any other neurophysiological parameter), exhibited respiratory PSG parameters characteristic of SAHS and had lower levels of uric acid, creatine and IGF-1 and higher levels of free thyroxine (T4).

Analysis of SAHS in obese versus non-obese children

Of all children with a diagnosis of SAHS ($n = 36$), 25 (69.4%) were not obese and 11 (30.6%) were obese.

Table 5 presents the characteristics of the SAHS-NOb and the SAHS-Ob groups; children in the SAHS-NOb group were younger and more likely to snore, differences that were significant in comparison with the SAHS-Ob group.

As for sleep hygiene and dietary habits (Table 5), children in the SAHS-Ob group slept fewer hours, and were less likely to use school lunch services and to have breakfast every day. When it came to PSG parameters (Tables 6 and 7), chil-

Table 5 General characteristics of the SAHS-non obese versus SAHS-obese subgroups.

	SAHS-non obese	SAHS-obese	<i>P</i>
M – F	64% -36%	55% -45%	.716
Age (range)	4.4(3.3-5.4)	8(4.4-10)	.010
BW pct (range)	28 (12.2-78.7)	70.5 (34-81.2)	.104
Tonsil grade			
0	0%	0%	
I-II	24%	55%	
III-IV	76%	45%	.124
Chervin test +	76%	64%	.454
Mouth breathing	80%	64%	.409
Somnolence	32%	18%	.688
Regular snoring	88%	45%	.012
Morning dry mouth	80%	55%	.224
SBP pct (range)	90 (50-95)	90 (90-99)	.278
DBP pct (range)	90 (90-95)	90 (50-90)	.063
Sleep duration, h (range)	10 (10-11)	10 (9.5 -10)	.038
PA, h (range)	7 (3.6-8)	5 (2.7-7)	.163
School lunch	48%	9%	.031
Breakfast daily	100%	64%	.006
5 meals/day	96%	73%	.076
Screen time, h (range)	1.3 (1-2)	2 (1-2)	.309

AHI, apnoea-hypopnoea index; BW, birth weight; DBP, diastolic blood pressure; F, female; h, hours; M, male; PA, physical activity; pct, percentile; SAHS, sleep apnoea-hypopnoea syndrome; SBP, systolic blood pressure.

dren in the SAHS-NOb group experienced more arousals and spent less time in stage 2 sleep relative to the total sleep duration, and had significantly higher AHI, supine AHI, central AHI and AI values and a significantly higher frequency of PETCO₂ greater than 50 mmHg compared to the SAHS-Ob group, and when it came to metabolic parameters (Table 8), children in the SAHS-Ob group had significantly higher glucose, creatinine, IGF-1, insulin and HOMA index values, and lower aspartate transaminase (AST) levels compared to the SAHS-NOb group.

Discussion

We conducted a prospective study to assess the clinical, polysomnographic and metabolic characteristics of a clin-

ical cohort of children with and without obesity referred for suspected SAHS. In this cohort, children with SAHS had a higher morning DBP, and the Chervin test could not discriminate between children with and without SAHS. In addition, children with obesity had abnormal sleep patterns and poor sleep hygiene and dietary habits, were more likely to have a family history of obesity and had higher glucose, insulin, HOMA index and triglyceride values.

Short sleep duration is associated with an increased risk of obesity,^{12,13} and the prevalence of sleep disorders has been found to be higher in obese children.¹⁴ In the sample under study, obese children exhibited sleep disturbances (shorter duration, lower efficiency, longer REM latency). At the same time, sleep deprivation causes daytime somnolence and fatigue that may result in a decrease in physical activity, which is consistent with the hours of physical

Table 6 Neurophysiological polysomnographic parameters in the SAHS-non obese versus SAHS-obese subgroups.

Nocturnal PSG	SAHS-non obese	IQR	SAHS-obese	IQR	<i>P</i>
Sleep duration, min	522	471.2-545.6	454.2	442-533	.069
Sleep efficiency, %	86.2	80.7-89.5	79	70.9-91.1	.186
NREM latency, min	29.5	16.2-39.7	30	10-65.5	.877
REM latency, min	86.5	70.2-121.2	130.5	89-154.5	.069
Intervening wake, %	8	6.9-12.3	10.9	7.5-22.9	.204
Stage 1, %	12.1	7.4-14.7	7.5	5.8-11.4	.052
Stage 2, %	30	24.5-36.6	37.8	32.7-45.9	.033
Stage 3, %	32.6	29.6-35.5	32.8	25.4-43.2	.981
REM sleep, %	25.3	22.5-28.6	21.3	18.4-30	.264
Arousals, <i>n</i>	140	99-177	85	50-112	.002
Arousal index	15.5	11.8-22.1	12.5	6.6-13	.022

IQR, interquartile range; Lat, latency; min, minutes; PSG, polysomnography; SAHS, sleep apnoea-hypopnoea syndrome; Wake, wakefulness.

activity reported by children in each group. Recent studies have analysed the association between sleep duration and lifestyle habits. Konstantions et al.¹⁵ found that insufficient sleep in children was associated with unhealthy dietary habits. The use of school lunch services has emerged as a protective factor against obesity. In our study, the proportion of children that used school lunch services was lower in the Ob group.^{5,16,17}

Several studies have found a clear association between the BMI of parents and the BMI of children,^{18,19} which was corroborated by our findings, as obesity in parents was more frequent in the obese group, which highlights the importance of this factor.

There are metabolic abnormalities associated with childhood obesity from an early age that present in isolation or as part of what is known as metabolic syndrome, as demonstrated by a collaborative study published by Martos et al.²⁰ Our study also found differences in parameters of carbohydrate metabolism (glucose and insulin levels and HOMA index) and lipid metabolism (TG levels), with higher values in obese children.

The use of questionnaires for screening of SAHS has been studied extensively. We used a validated version of the Chervin questionnaire in Spanish. In the sample under study, the questionnaire results were positive in 72% of children with SAHS compared to 68% of children without SAHS

(*P* = .689), which brings into question the use of questionnaires for diagnosis; in this regard, a recent meta-analysis analysed the accuracy of the Chervin test²¹ and found that it offered a lower sensitivity and specificity than previously reported and that it was not useful for assessment of individuals with obesity, in agreement with other studies.³

Of all the health problems associated with SAHS, cardiovascular disease is among the most important, and the association between SAHS and high BP in children has been subject to extensive study, although the data published to date are contradictory. In our study we found significantly higher morning DBP values in children with SAHS. Similarly, several authors have found that BP values increase with the severity of SAHS.^{22,23} Furthermore, studies that used 24-h ambulatory BP monitoring found an absence of the nocturnal dipping in BP and a marked increase in the morning BP associated with SAHS,^{24,25} and therefore a higher cardiovascular risk.

On the other hand, the comparison of neurophysiological parameters in children with and without SAHS only found differences in the number of arousals, which is why use of respiratory polygraphy, which does not monitor these parameters, is currently recommended for diagnosis of SAHS.²⁶

Another important aspect is the association between SAHS and abnormal growth; in this regard, a study con-

Table 7 Respiratory polysomnographic parameters in the SAHS-non obese versus SAHS-obese subgroups.

Nocturnal PSG	SAHS-non obese	IQR	SAHS-obese	IQR	P
Central Ap. (n)	9	3.5-15	3	0-10	.056
Obstructive Ap. (n)	20	5-80	1	0-23	.014
Mixed Ap. (n)	0	0-3	0	0-2	.378
Hypopnoea (n)	58	18.5-95	27	13-63	.144
RERAs (n)	34	18-58	25	9-30	.164
AHI	13.1	4.9-23.1	5.4	3.6-8	.041
REM AHI	14.3	5.4-38.3	8.5	2.8-10.8	.131
NREM AHI	11.9	3.2-19.7	6	3.5-7.8	.140
Supine AHI	16.3	8.6-34.8	7.3	5.1-12.8	.013
oAHI	10.6	4.3-17.6	4.1	3.5-7.7	.083
cAHI	1.15	0.5-1.9	0.3	0-1.2	.030
RDI	17.6	9.1-27.2	8	6.7-12.7	.057
Mean SatO ₂ (%)	96.8	96.2-97.2	96.6	96.1-96.7	.173
SatO ₂ min. (%)	85	81-88.5	88	84-90	.286
ODI (%)	7.4	3.9-13.5	6.7	2.1-10.3	.372
PETCO ₂ , mmHg	3	0-11.3	0	0-0.2	.023

AHI, apnoea-hypopnoea index; Ap, apnoea; cAHI, central apnoea-hypopnoea index; NREM AHI, non-REM sleep apnoea-hypopnoea index; oAHI, obstructive apnoea-hypopnoea index; ODI, oxygen desaturation index; PETCO₂, partial pressure of end tidal CO₂; RDI, respiratory disturbance index; REM AHI, REM sleep apnoea-hypopnoea index; RERA, respiratory event-related arousal; SAHS, sleep apnoea-hypopnoea syndrome; SatO₂ min, minimum oxygen saturation.

ducted in children with SAHS and with primary snoring found lower concentrations of insulin-like growth factor binding protein-3 (IGFBP-3), a transport protein, although it found no differences in the concentration of IGF-1.²⁷ When we compared children with and without SAHS in our study, we only found differences in the levels of IGF-1, creatinine, uric acid and free T₄, although these differences could be explained by the age difference between the groups.

In the analysis of the SAHS group, we found that the SAHS-NOb subgroup was younger in age, had a higher prevalence of regular snoring and had a higher AHI compared to the SAHS-Ob subgroup. We did not find differences in tonsil size between groups, although a grade III-IV size was observed in 76% of the SAHS-NOb subgroup compared to 45% of the SAHS-Ob subgroup, which may be explained by the higher degree of adenotonsillar hypertrophy in the younger age group doc-

umented in the literature.^{1,2} Still, the fact remains that not all children with adenotonsillar hypertrophy develop SAHS.

Although SAHS has been identified as a risk factor for insulin resistance in adults, the association in children unclear. Studies performed mainly in adolescents have found an association between metabolic syndrome and SAHS, whereas in younger children, SAHS is associated with an increase in insulin resistance when SAHS co-occurs with obesity.^{2,28} In our study, we found more carbohydrate metabolism abnormalities in the SAHS-Ob group, abnormalities that were present in the Ob group, suggesting that insulin resistance is mainly determined by obesity with a lesser contribution of SAHS, as described by other authors.²⁹ We also found a higher median HOMA index in the SAHS-Ob group compared to the subset of children with obesity and without SAHS, which suggests that SAHS enhances the effect

Table 8 Metabolic parameters in the SAHS-non obese versus SAHS-obese subgroups.

Laboratory results	SAHS-non obese	IQR	SAHS-obese	IQR	<i>P</i>
Glucose, mg/dL	82	78-87	86	82-91	.039
Creatinine, mg/dL	0.3	0.3-0.4	0.5	0.3-0.5	.001
AST, IU/L	28	26-31.5	21	19-25	<.001
ALT, IU/L	15	14-19	16	14-19	.882
TG, mg/dL	49	40-67	57	46-135	.141
Total cholesterol, mg/dL	168	140-182	157	150-171	.768
CPR, mg/dL	0	0-3	1	0-2	.653
Vitamin D, ng/mL	27.8	20.1-36.4	23.5	12.9-29.1	.060
Ferritin, ng/mL	40	30.3-49	43	22-60	.768
IGF-1, ng/mL	76	54-120	158	127-209	<.001
Insulin, μ U/L	4.8	2.8-6.4	20.1	12.8-27.9	<.001
HOMA	1	0.5-1.5	4.6	2.6-6.1	<.001

ALT, alanine aminotransferase; AST, aspartate transaminase; CPR, C-reactive protein; HOMA, insulin resistance index; IGF-1, insulin-like growth factor-1; IQR, interquartile range; SAHS, sleep apnoea-hypopnoea syndrome; TG, triglycerides.

of obesity, a phenomenon observed in previous studies with larger samples.³⁰

Another salient finding was the difference in liver enzyme levels in the comparison of the SAHS-NOB and SAHS-Ob subgroups, with higher levels in the non-obese subgroup ($P < .001$), which also had a higher AHI ($P = .041$). Our findings on this aspect are consistent with the previous literature, as the presence and severity of SAHS is associated with liver enzyme elevation and non-alcoholic fatty liver disease independently of the BMI.³¹

One potential limitation of the study is that it was conducted in a cohort of children with and without obesity referred for suspected SAHS, so that they were not representative of the entire paediatric population with obesity, in which SAHS is subject to a low level of suspicion and underdiagnosed, as evinced by the previous literature.³ Another limitation is the small sample size in the analysis of the SAHS-NOB vs SAHS-Ob subgroups. In relation to this, another possible limitation is the reason for referral: the presence of snoring. In our study, snoring had been documented at the time of referral in 62% of children without SAHS vs 75% of children with SAHS ($P = .066$), while in the sleep study (snoring detected by pressure transducers and/or witnessed in the laboratory) it was detected in 45% of children without SAHS vs 77% of children with SAHS ($P = .017$), so that while snoring is a warning sign, emphasis must be placed on identifying other symptoms suggestive of SAHS, especially in older or obese children.

Conclusions

Our study found that SAHS presented differently in 2 paediatric phenotypes, with and without obesity, with different findings based on age and clinical, polysomnographic and metabolic characteristics.

Children with obesity had abnormal sleep patterns and poor sleep hygiene and dietary habits, in addition to abnormalities in carbohydrate and lipid metabolism.

We found an increased DBP in children with SAHS, which is indicative of an increased cardiovascular risk.

Our findings also highlight the need to improve the questionnaires used to detect SAHS and to develop specific instruments to assess paediatric patients with obesity.

Thus, it is important to be aware of the increased risk of morbidity associated with SAHS in the presence of obesity, and training programmes and awareness campaigns should be implemented at the primary care level to improve knowledge of SAHS in the context of childhood obesity. Such programmes would counteract the tendency to underdiagnose SAHS, contributing to its early treatment and therefore to reducing the morbidity associated with this condition.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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References

- Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2012;130:576–84.
- Alonso Álvarez ML, Canet T, Cubell Alarco M, Estivill E, Fernández Julián E, Gozal D, et al. Documento de Consenso del síndrome de apneas hipopneas durante el sueño en niños (versión completa). *Arch Bronconeumol*. 2011;47:2–18.
- Alonso Álvarez ML, Cordero Guevara JA, Terán Santos J, González Martínez M, Jurado-Luque MJ, Corral-Peñañiel J, et al. Obstructive sleep apnea in obese community-dwelling children: the NANOS study. *Sleep*. 2014;37:943–9.
- World Health Organization. Obesity: preventing and managing the global epidemic: report on a WHO Consultation (WHO Technical Report Series 894). Geneva, Switzerland: World Health Organization; 2000.
- Estudio ALADINO 2015: Estudio de Vigilancia del Crecimiento, Alimentación, Actividad Física, Desarrollo Infantil y Obesidad en España 2015. Agencia Española de Consumo, Seguridad Alimentaria y Nutrición. Ministerio de Sanidad, Servicios Sociales e Igualdad. Madrid. 2016.
- Sobradillo B, Aguirre A, Aresti U, Bilbao A, Fernández Ramos C, Lizárraga A, et al. Curvas y tablas de crecimiento. Estudios longitudinal y transversal Fundación F. Orbegozo. In: Patrones de crecimiento y desarrollo en España. Atlas de graficas y tablas. Madrid: Ergon; 2004.
- Tomás Vila M, Miralles Torres A, Beseler Soto B. Versión española del Pediatric Sleep Questionnaire. Un instrumento útil en la investigación de los trastornos del sueño en la infancia. Análisis de su fiabilidad. *An Pediatr (Barc)*. 2007;66:121–8.
- Chervin RD, Hedger K, Dillon JE, Pituch KJ. Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. *Sleep Med*. 2000;1:21–32.
- Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens*. 2016;34:1887–920.
- Brodsky L, Moore L, Stanievich J. A comparison of tonsillar size and oropharyngeal, dimensions in children with obstructive adenotonsillar hypertrophy. *Int J Pediatr Otorhinolaryngol*. 1987;13:149–56.
- Berry RB, Brooks R, Gamaldo CE, Harding SM, Marcus CL, Vaughn BV, et al. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, version 2.0. Darien, Illinois: American Academy of Sleep Medicine; 2012.
- Li L, Zhang S, Huang Y, Chen K. Sleep duration and obesity in children: a systematic review and meta-analysis of prospective cohort studies. *J Paediatr Child Health*. 2017;53:378–85.
- Miller MA, Kruisbrink M, Wallace J, Ji C, Cappuccio FP. Sleep duration and incidence of obesity in infants, children, and adolescents: a systematic review and meta-analysis of prospective studies. *Sleep*. 2018;41(4).
- Carriere C, Coste O, Meiffred-Drouet MC, Barat P, Thibault H. Sleep disorders in obese children are not limited to obstructive sleep apnoea syndrome. *Acta Paediatr Int J Paediatr*. 2018;107:658–65.
- Tambalis KD, Panagiotakos DB, Psarra G, Sidossis LS. Insufficient sleep in children is associated with poor diet, obesity and more screen time. *J Clin Sleep Med*. 2018;14:1689–96.
- Aranceta Bartrina J, Pérez Rodrigo C, Serra Majemby L, Delgado Rubio A. Hábitos alimentarios de los alumnos usuarios de comedores escolares en España. Estudio «Dime Cómo Comes». *Aten Primaria*. 2004;33:131–9.
- Ministerio de Sanidad, Política Social e Igualdad, Available from: <http://www.aesan.mssi.gob.es/AECOSAN/web/nutricion/seccion/educaNAOS.shtml>, 2017.
- Law C, Power C, Lo Conte R, Li L. Intergenerational influences on childhood body mass index: the effect of parental body mass index trajectories. *Am J Clin Nutr*. 2008;89:551–7.
- Martínez Villanueva J, González Leal R, Argente J, Martos Moreno GA. La obesidad parental se asocia con la gravedad de la obesidad infantil y de sus comorbilidades. *An Pediatr (Barc)*. 2019;90:224–31.
- Martos Moreno GA, Gil Campos M, Bueno G, Bahillo P, Bernal S, Felio A, et al. Las alteraciones metabólicas asociadas a la obesidad están ya presentes en los primeros años de vida: Estudio colaborativo español. *Nutr Hosp*. 2014;30:787–93.
- Michelet D, Julien-Marsollier F, Vacher T, Bellon M, Skhiri A, Bruneau B, et al. Accuracy of the sleep-related breathing disorder scale to diagnose obstructive sleep apnea in children: a meta-analysis. *Sleep Med*. 2019;54:78–85.
- Nisbet LC, Yiallourou SR, Walter LM, Horne RSC. Blood pressure regulation, autonomic control and sleep disordered breathing in children. *Sleep Med Rev*. 2014;18:179–89.
- Li AM, Au CT, Sung RYT, Ho C, Ng PC, Fok TF, et al. Ambulatory blood pressure in children with obstructive sleep apnoea: a community based study. *Thorax*. 2008;63:803–9.
- Amin RS, Carroll JL, Jeffries JL, Grone C, Bean JA, Chini B, et al. Twenty-four-hour ambulatory blood pressure in children with sleep-disordered breathing. *Am J Respir Crit Care Med*. 2004;169:950–6.
- Weber SA, Santos VJ, Semenzati GdO, Martin LC. Ambulatory blood pressure monitoring in children with obstructive sleep apnea and primary snoring. *Int J Pediatr Otorhinolaryngol*. 2012;76:787–90.
- Alonso-Álvarez ML, Terán-Santos J, Ordax Carbajo E, Cordero-Guevara JA, Navazo-Egüia AI, Kheirandish-Gozal L, et al. Reliability of home respiratory polygraphy for the diagnosis of sleep apnea in children. *Chest*. 2015;147:1020–8.
- Nieminen P, Löppönen T, Tolonen U, Lanning P, Knip M, Löppönen H. Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. *Pediatrics*. 2002;109:55.
- Alonso Álvarez ML, Terán Santos J, Gonzalez Martinez M, Cordero Guevara JA, Jurado Luque MJ, Corral Peñañiel J, et al. * The Spanish Sleep Network, Metabolic biomarkers in community obese children: effect of obstructive sleep apnea and its treatment. *Sleep Med*. 2017;37:1–9.
- Tauman R, O’Brien LM, Ivanenko A, Gozal D. Obesity rather than severity of sleep-disordered breathing as the major determinant

- of insulin resistance and altered lipidemia in snoring children. *Pediatrics*. 2005;116:66–73.
30. Gozal D, Capdevila OS, Kheirandish-Gozal L. Metabolic alterations and systemic inflammation in obstructive sleep apnea among nonobese and obese prepubertal children. *Am J Respir Crit Care Med*. 2008;177:1142–9.
31. Nobili V, Cutrera R, Liccardo D, Pavone M, Devito R, Giorgio V, et al. Obstructive sleep apnea syndrome affects liver histology and inflammatory cell activation in pediatric nonalcoholic fatty liver disease, regardless of obesity/insulin resistance. *Am J Respir Crit Care Med*. 2013;189:66–76.