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Association of Visceral Adiposity and Systemic Inflammation with Sleep Disordered Breathing in Normal Weight, Never Obese Adolescents

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Abstract

Objective/Background: While obesity is a known risk factor for sleep disordered breathing (SDB), a large proportion of children with SDB are not overweight as per body mass index percentile (BMI%) criteria. This study aimed to examine whether premorbid or concurrent adiposity phenotypes and inflammation are associated with SDB in normal weight youth.

Patients/Methods: A total of 242 persistently non-overweight (BMI%<85) subjects from the Penn State Child Cohort (N=421, 5–12y at baseline and 12–23y at follow-up), were studied. The apnea/hypopnea index (AHI) was ascertained via polysomnography at both time points. At follow-up, a DXA scan assessed android and gynoid distribution and subcutaneous (SAT) and visceral (VAT) adiposity composition, while a fasting blood draw was assayed for C-reactive protein (CRP) and interleukin-6 (IL-6) levels. Multivariable linear regression models with AHI at follow-up as primary outcome were adjusted for sex, race, adenotonsillectomy, age and AHI at baseline.

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Credit Author Statement

Jacqueline M. Danisi, MS, had access to the de-identified dataset, performed the statistical analyses, interpreted the results and drafted the manuscript.

Julio Fernandez-Mendoza, PhD, provided with the original de-identified dataset, supervised the primary statistical analyses, performed any revision to the statistical analyses, interpreted the results and drafted the manuscript.

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6. DECLARATION OF INTERESTS

Declarations of interest: none.

Results and Conclusions: Increased waist circumference (β=0.227, p=0.001) at baseline, but not BMI%, neck or hip circumference, were significantly associated with a higher AHI at follow-up. VAT (β=0.309, p<0.001), IL-6 (β=0.243, p<0.001), SAT (β=0.235, p=0.013), CRP (β=0.221, p=0.001), and an android distribution (β=0.196, p=0.003) at follow-up were significantly associated with a higher AHI at follow-up. Childhood central adiposity predicts SDB in adolescence, even in individuals who have never been overweight since childhood as per BMI criteria. Visceral adiposity and inflammation are concurrent to adolescent SDB, which supports the clinical utility of these biomarkers in predicting its associated cardiometabolic risk.

Keywords

Childhood obesity; visceral adipose tissue; sleep disordered breathing; inflammation; normal weight

1. INTRODUCTION

Sleep disordered breathing (SDB) is a prevalent sleep disorder characterized by obstruction of the upper airway during periods of sleep. It is estimated that 1–4% of the general pediatric population, and 4–11% of adolescents have moderate-to-severe SDB.[1] Although SDB in children is thought to be the result of anatomical abnormalities of the upper airway, such as enlarged tonsils and/or adenoids, obesity is recognized as a strong risk factor for the development of SDB. It is believed that cessation of breathing is most commonly a result of excess fat and tissue compressing the pharynx, preventing breathing mechanisms to occur in overweight and obese individuals.[2,3]

Unfortunately, pediatric obesity is steadily increasing, leading to a parallel increase in adverse cardiometabolic morbidities. By 2014, more than 17% of 2–19 year olds were categorized as obese by body mass index (BMI) percentile for sex and age.[4] Although obesity is a strong risk factor for SDB, a significant proportion of children with SDB are not obese or overweight.[5,6,7] Adiposity distribution can have varying effects on the individual depending upon the patterning of this distribution, and this pattern may not be observed by clinical methods such as BMI. It has been shown that in non-obese middle-aged adults, central and visceral adiposity are predominant risk factors for SDB.[8] Thus, it is possible that children who are not characterized as overweight or obese by their BMI percentile may still be at risk of SDB and cardiometabolic morbidity due to their distribution of adipose tissue, especially if they exhibit central adiposity.

Central adiposity is defined as the accumulation of adipose tissue in the android region, including subcutaneous (SAT) and visceral (VAT) adipose tissues.[9] It is usually measured taking a waist circumference via a tape measure. Central adiposity poses risks to an individual's health partly due to the large accumulation of VAT. Unlike SAT or gynoid adipose tissue distribution, VAT is deep within the abdomen surrounding the internal organs, and is considered itself to be a metabolically-active organ.[10] The unique position of VAT in respect to the liver and surrounding endocrine organs explains its higher metabolic and inflammatory burden, as indexed by higher levels of C-reactive protein (CRP). CRP is an acute-phase protein of hepatic origin that increases following the secretion of the pro-

inflammatory cytokine interleukin-6 (IL-6) by macrophages and T cells as well as adipocytes[9]. This increased risk for cardiometabolic morbidity, therefore, places precedence on the distribution of adipose tissue, specifically central adiposity, and not solely on the BMI of the patient like typically assumed. Therefore, although some adolescents may have never been clinically categorized as overweight or obese, if they have increased abdominal adiposity, they may be at increased risk of adverse health outcomes. However, this hypothesis needs yet to be tested as it pertains to SDB.

Thus, the aim of this study was to examine whether central adiposity is a predictor of apnea/hypopnea index (AHI) in adolescents who have never been overweight since childhood. Never overweight children followed-up as adolescents provide a unique opportunity to examine premorbid associations as well as concurrent phenotypes typically missed in routine clinical practice. We hypothesized that increased 1) childhood waist circumference and 2) adolescent visceral adiposity and pro-inflammatory cytokines are associated with a greater AHI in adolescence and greater increase in AHI from baseline to adolescence, in otherwise non-overweight youth based on BMI percentile criteria.

2. METHODS

2.1 Sample

The Penn State Child Cohort (PSCC)[11] is a random, general population sample of 700 children between ages 5 and 12 years old (mean age 8.7 ± 1.7 years old), of whom 421 were followed up 8.4 years later as adolescents (mean age 17.0 ± 2.2 years old, 53.9% male, 93.6% non-Hispanic and 6.4% Hispanic, and 82.5% Caucasian, 12.6% Black/African American, and 2.9% American Indian or Native Hawaiian/Asian). The PSCC was designed as a two-phase study. During Phase I, 7,312 children from 18 public elementary schools within three Dauphin County, Pennsylvania, school districts were sent home with a questionnaire completed by a parent on their child's sleep and behavior; 5,740 surveys were returned (79% response rate). During Phase II, based on stratification for grade, sex, and SDB risk by the questionnaire, 1,000 children were randomly selected to spend a night at the Penn State College of Medicine Clinical Research Center; 700 children participated (70% response rate). Out of the 700 subjects, 421 completed a follow-up examination about 8.4 years later (60% response rate). The loss to follow-up was mainly due to subjects moving out of central Pennsylvania. However, no major difference in baseline characteristics was observed between subjects who did and did not participate.[12] The participants underwent a standard in-lab sleep recording and a detailed clinical history and physical examination both at baseline and at follow-up. Additionally, subjects underwent a dual-energy x-ray absorptiometry (DXA) scan and fasting blood sampling at follow-up.[9]

2.2 Physical Examination

At their baseline and follow-up visits in the laboratory, all participants underwent a physical examination, during which height (stadiometer model 242, SECA; Hanover, MD), weight (model 758C, Cardinal Manufacturing; Webb City, MO), and neck, waist and hip circumferences via tape measure were recorded according to Centers for Disease Control Criteria.[13] BMI was calculated (in kg/m^2) and converted to a percentile according to a

formula based on the Centers for Disease Control's sex-specific BMI-for-age growth charts.[14] Subjects with a BMI percentile ≥85% at either baseline or follow-up were not included in this study. The primary analyses focused on the 242 subjects with a BMI percentile <85% at both baseline and follow-up. Sensitivity analyses further excluded 17 subjects with a BMI percentile <5% to identify pure "persistently normal weight" children. At both baseline and follow-up, a history of surgical removal of tonsils and/or adenoids was recorded from the parent (baseline) and the parent or the subject (follow-up), and a lifetime history of adenotonsillectomy was ascertained.[12] Only at follow-up, pubertal development (Tanner staging) was determined via a self-administered rating scale.[15] Participants also underwent a whole-body DXA scan using a Hologic Discovery W scanner (Hologic, Waltham, MA; 195 × 65 cm field of view) to obtain a precise measure of body adiposity. Regions of interest included android and gynoid ratios and SAT and VAT. These regions were identified by Hologic APEX 4.0 software (Hologic, Bedford, MA) and visually verified by an experienced technician; more detailed descriptions of these measures can be found elsewhere.[10]

2.3 Sleep Laboratory

All participants underwent a 9-hour polysomnography (PSG) recording in a sound-attenuated, light- and temperature-controlled room with a comfortable, bedroom-like atmosphere at both baseline and follow-up. Each subject was continuously monitored from 22:00 h until 7:00 h using 14-channel recordings of electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG). Respiration was monitored via nasal pressure (Pro-Tech PTAF Lite; Mukilteo, WA), thermocouple (Salter Labs; Lake Forest, IL), and thoracic/abdominal strain gauges (Model 1312, Sleepmate Technologies; Midlothian, VA). Hemoglobin oxygen saturation (SpO_2) was assessed using a pulse oximeter placed on the index finger (Model 3011 Xpod, Nonin Medical, Inc.; Plymouth, MN). Snoring sounds were monitored via a sensor attached to the throat. All data were recorded using Twin Recording & Analysis software (Grass-Telefactor; West Warwick, RI). Visual sleep stage scoring was conducted by registered polysomnography technologists according to standardized criteria.[16] AHI was ascertained as number of obstructive apneas and hypopneas per hour of sleep according to standardized criteria.[1,11,12]

2.4 Blood Draw and Assay Procedures

Upon awakening (7:00) from the PSG study at follow-up only, blood samples were collected in EDTA-containing tubes, then spun for 10 min at 3000 RPM. Plasma was aliquoted into cryotubes and stored at −80°C until assayed. High-sensitivity C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNFα), leptin, and adiponectin were measured via enzyme-linked immunosorbent assay (ELISA; R&D Systems; Minneapolis, MN). The intra- and interassay coefficients of variation for CRP were 5.5% and 6.5% for samples collected at baseline, and 5.8% and 5.3% for samples collected at follow-up. The intra- and interassay coefficients for variation were 4.7% and 5.1% respectively (IL-6), 4.6% and 4.9% (TNFα), 6.5% and 7.0% (leptin), and 5.6% and 5.6% (adiponectin). The lower detection limits were 0.010 ng/mL (CRP), 0.039 pg/mL (IL-6), 0.106 pg/mL (TNFα), 7.2 pg/mL (leptin), and 0.25 ng/mL (adiponectin). All samples and standards were run in duplicate.

2.5 Statistical Analyses

The primary outcome of this study was AHI at follow-up as a continuous variable. Secondary outcomes included the change in AHI from baseline to follow-up (ΔAHI) and clinically defined SDB groups. First, we conducted univariate linear regression models between study variables and the continuous outcome of AHI at follow-up. Second, based on the significant univariate associations, we conducted multivariable linear regression (MLR) models that further adjusted for the potential effect of the co-variables sex, race, adenotonsillectomy, and age and AHI at baseline. Third, a stepwise MLR model with all previous significant variables (backward elimination) and the co-variables sex, race, adenotonsillectomy, and age and AHI at baseline (forced entry) examined which of these anthropometric- and inflammatory-related variables were independently associated with AHI at follow-up. An alternative MLR model with the secondary outcome of ΔAHI as the dependent variable was also conducted. Sensitivity analyses were conducted after excluding 17 subjects with a BMI percentile <5% at any time point. Finally, based on the significant associations found with AHI at follow-up, we conducted analyses of variance (ANOVA) to examine mean differences in those continuous variables among categorically-defined, clinically meaningful groups of SDB consisting of no SDB (AHI<2 and no snoring), primary snoring (AHI<2 and snoring), 2≤AHI<5, and AHI≥5.[12] All analyses were conducted with SPSS version 24.

3. RESULTS

3.1 Demographic, clinical and sleep characteristics of the sample

This subsample from the PSCC was comprised of 242 never overweight subjects with an average BMI percentile of 44.9 ± 22.5 at baseline and 48.4 ± 28.2 at follow-up. The demographic and clinical characteristics of these 5–12 year old children at baseline (49.2% female, 18.2% racial/ethnic minority) followed-up after 7.7 ± 1.4 years as 12–23 year old adolescents are presented in Table 1. Their average AHI at baseline was 0.7 ± 0.9 events per hour of sleep (range, 0.0–5.3) and 72.7% did not have any form of SDB at baseline, while 19.8%, 6.2% and 1.2% had primary snoring, 2≤AHI<5 and AHI≥5, respectively. The average AHI at follow-up was 2.3 ± 6.3 events per hour of sleep (range, 0.0–91.9) and 42.1% did not have any form of SDB at follow-up, while 28.1%, 23.6% and 6.2% had primary snoring, 2≤AHI<5 and AHI≥5, respectively. The average SpO2 at baseline was 93.0 ± 4.5, while at follow-up it was 91.5 ± 5.2. A total of 9.9% of the sample had a lifetime history of adenotonsillectomy.

3.2 Association of demographic, clinical and sleep variables with AHI

As shown in Supplemental Table 1, older age and Tanner stage at follow-up were significantly associated with greater AHI outcomes. Chronic cough at baseline was significantly associated with greater AHI at baseline, while a lifetime history of adenotonsillectomy was associated with a greater AHI at follow-up and ΔAHI. In contrast, neither enlarged tonsils nor tonsil inflammation at baseline were significantly associated with greater AHI at either time point.

3.3 Association of anthropometric variables and immune biomarkers with AHI

Univariate analyses showed that neither weight, BMI, neck or hip circumference at baseline were significantly associated with AHI at follow-up (Table 2). However, waist circumference at baseline was significantly associated with a greater AHI at follow-up (Table 2) and greater ΔAHI (Supplemental Table 1). Consistently, a waist circumference percentile ≥ 85% at baseline was significantly associated with a greater AHI at follow-up (β=0.236, p<0.001) and greater ΔAHI (β=0.245, p<0.001). Android/whole body ratio, SAT, and VAT at follow-up were all significantly associated with a greater AHI at follow-up (Table 2) and a greater ΔAHI (Supplemental Table 1); in fact, VAT showed a stronger cross-sectional association (β>0.3) than SAT (β<0.2) with AHI. Higher CRP and IL-6 levels at follow-up were also significantly associated with a greater AHI at follow-up (Table 2) or with ΔAHI (Supplemental Table 1).

3.4 Multivariable analyses of anthropometric and inflammatory factors associated with AHI in adolescence

Table 2 shows multivariable modelling of the significant associations presented above. After adjusting for sex, race, adenotonsillectomy, and age and AHI at baseline (Model 1), waist circumference (β=0.157, p=0.038) and waist circumference percentile ≥ 85% (β=0.227, p=0.001) at baseline remained significantly (P<0.05) associated with a higher AHI at follow-up. Similarly, VAT (β=0.309, p<0.001), IL-6 (β=0.243, p<0.001), SAT (β=0.235, p=0.013), CRP (β=0.221, p=0.001), and android/whole body ratio (β=0.196, p=0.003) at follow-up also remained significantly associated with a higher AHI at follow-up after adjusting for the same co-variables (Model 1). A stepwise MLR model with backward elimination (Model 2) showed that VAT (β=0.249), IL-6 (β=0.189), baseline waist circumference percentile ≥ 85% (β=0.191), and CRP (β=0.163) were independently associated with a higher AHI at follow-up. An alternative stepwise MLR model also showed that VAT (β=0.246), baseline waist circumference percentile ≥ 85% (β=0.189), IL-6 (β=0.187) and CRP (β=0.162) were independently associated with ΔAHI. As shown in Supplemental Table 2, these findings remained significant, in the same direction and with similar strength of association even after excluding those few subjects with a BMI percentile <5% (n=17) to identify "persistently normal weight" children.

3.5 Categorical analyses with clinically meaningful SDB groups

Based on the significant associations above, we also examined the data based on categorically defined SDB groups using clinical AHI cut-offs.[12] As shown in Table 3, all baseline variables remained significant for SDB severity groups, with adolescents with an AHI≥5 being the oldest and having the largest waist circumference at baseline. Weight and waist circumference at follow-up were also found to be significantly increased across adolescent SDB groups, with adolescents with an AHI≥5 being the heaviest and having the largest waist circumference. In regard to adipose tissue distribution and composition at follow-up, android/whole body ratio and VAT were linearly increased across adolescent SDB groups, while gynoid/whole body ratio and SAT were not. Additionally, CRP levels at follow-up were significantly increased across adolescent SDB groups, with adolescents with an AHI≥5 having the highest CRP levels.

4. DISCUSSION

This is the first study to demonstrate that central adiposity in childhood is a strong predictor of SDB in adolescence, even in youth who have never been overweight since childhood as per BMI criteria. The finding remains even after identifying pure “persistently normal weight” children by excluding those with underweight BMI criteria at any time point. The risk of developing SDB in adolescence is not solely contingent upon overall obesity and BMI percentile categorizations, but rather, is found based on specific adipose tissue distribution and composition. Our study demonstrated that increased android and visceral adiposity and systemic inflammation are strong correlates of SDB in otherwise normal weight adolescents, which supports the clinical utility of these biomarkers in predicting the cardiometabolic risk associated with adolescent SDB.

We found that youth’s waist circumference, but not absolute weight, was significantly associated with a greater increase in AHI from childhood to adolescence and a greater AHI in adolescence. This association remained strong and significant when childhood waist circumference was categorized based on percentile for age-and-sex. This finding suggests that subclinical levels of central adiposity, as measured by waist circumference, are longitudinally associated with an increased risk of SDB in adolescence well before the child or adolescent becomes overweight or obese as per BMI criteria. This finding was further supported by the DXA scan data showing that an android distribution and high VAT composition were cross-sectionally associated with a greater AHI in adolescence. Interestingly, SAT was not associated with a greater AHI at adolescence after multivariable adjustments. Therefore, the relationship between increased waist circumference in childhood and development of SDB in adolescence may stem from an increase in VAT during this transitional period. Together, these data further support a closer link between android and visceral adiposity with SDB, independent of global obesity as per BMI criteria, than previously believed.

Importantly, VAT, unlike SAT, is an inflammatory organ associated with systemic inflammation in individuals with obesity.[17] The finding that CRP and IL-6 levels were cross-sectionally associated with a greater AHI even in these adolescents who had never been overweight since childhood supports that CRP levels can serve as biomarkers of the severity of SDB as early as adolescence.[18] Future studies should examine whether CRP levels, rather than AHI levels, can reliably predict the development of cardiometabolic morbidity (e.g., hypertension, type 2 diabetes) in these adolescents with SDB, particularly those with the more severe phenotype (i.e., AHI≥5) which represented 6.2% of these otherwise normal weight adolescents.

The findings of our study should be interpreted in light of some potential limitations. First, the lack of an evaluation between childhood and adolescence precludes ascertaining whether any of these children had become overweight or obese at any time point before the follow-up. However, our and others data[19,20] indicate that childhood overweight, particularly childhood obesity, is highly persistent in the transition to adolescence and that a recurrent course (i.e., normal weight → obese → normal weight) is highly unlikely to occur during this developmental period.[21,22] Second, the DXA scan and inflammatory biomarkers were

only assessed at follow-up; thus, the change in body fat distribution and composition or in inflammation could not be examined from baseline and compared to that measured at follow-up. For this reason, these data should be interpreted as correlates rather than predictors.

In conclusion, this study demonstrates that subclinical markers of central adiposity in childhood are strong predictors of SDB in adolescence, even in youth who have been persistently normal weight since childhood as per BMI standards. These data support the clinical utility of simple measures of central adiposity in childhood to aid in predicting the risk of future development of SDB in the transition to adolescence. Our data also support the collection of inflammatory biomarkers in adolescence, and potentially as early as childhood, to better ascertain the severity and impact of SDB on the development of cardiometabolic morbidity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

AHI	apnea/hypopnea index
BMI	body mass index
CRP	C-reactive protein
DXA	dual-energy x-ray absorptiometry
EEG	electroencephalogram
EMG	electromyogram
EOG	electrooculogram
IL-6	interleukin-6
MLR	multivariable linear regression
PSCC	Penn State Child Cohort
PSG	polysomnography
SAT	subcutaneous adipose tissue
SDB	sleep disordered breathing

SpO_2	hemoglobin oxygen saturation
TNFα	tumor necrosis factor alpha
VAT	visceral adipose tissue

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HIGHLIGHTS

- Childhood waist circumference longitudinally associated with sleep disordered breathing in normal weight adolescents
- Visceral adipose tissue cross-sectionally associated with sleep disordered breathing in normal weight adolescents
- CRP levels independently associated with sleep disordered breathing in normal weight adolescents

Table 1.

Characteristics of the study sample in childhood (baseline) and adolescence (follow-up)

	Baseline	Follow-up	p-value[a]
Age, years	8.6(1.7)	16.3 (2.2)	<**0.001**
Tanner stage, score	---	4.1 (0.8)	---
Wheezing, %	9.6%	14%	0.068
Chronic Cough, %	5.8%	5.0%	0.671
Cough with exercise, %	9.6%	8.3%	0.494
Allergies, %	61.8%	58.3%	0.528
Enlarged tonsils, %	33.8%	---	---
Tonsils inflammation, %	1.8%	---	---
Cervical adenopathy, %	27.4%	---	---
Height, cm	133.9(10.9)	168.1 (9.8)	<**0.001**
Weight, kg	29.4 (6.4)	59.2(10.0)	<**0.001**
zBMI, z-score	−0.6 (0.8)	−0.1 (0.8)	**0.028**
BMI%, percentile	44.9 (22.5)	48.4(24.1)	<**0.001**
Neck circumference, cm	27.9 (4.2)	34.2(5.1)	<**0.001**
Waist circumference, cm	59.9(5.1)	73.2(7.1)	<**0.001**
Hips circumference, cm	68.7 (8.7)	84.1 (9.3)	<**0.001**
Gynoid/whole ratio, %	---	18.6 (2.5)	---
Android/whole ratio, %	---	5.5(1.0)	---
Subcutaneous tissue, cm^2	---	139.7(85.9)	---
Visceral tissue, cm^2	---	38.4(15.0)	---
CRP, mg/L	---	0.7 (0.6)	---
IL-6, pg/mL	---	1.0(0.9)	---
TNF-α, pg/mL	---	1.8(1.2)	---
Leptin, ng/mL	---	8.4 (8.5)	---
Adiponectin, μg/mL	---	8.4 (4.9)	---
Total sleep time, min	461.1 (44.3)	447.8 (49.0)	<**0.001**
Stage N1,%	3.3 (2.7)	0.9(1.0)	<**0.001**
Stage 2, %	46.3 (10.8)	53.2 (10.2)	<**0.001**
Stage 3, %	30.1 (10.2)	27.2 (9.5)	<**0.001**
Stage R, %	20.4 (5.2)	18.6(4.7)	<**0.001**
PLMI, events/hour	0.8 (4.0)	4.5 (6.8)	<**0.001**
AHI, events/hour	0.7 (0.9)	2.3 (6.3)	<**0.001**

Data are mean (standard deviation) for continuous variable and percentage for categorical variables. [b] Bold p-values indicate statistical significance at $p \leq 0.05$. Participants identified their race/ethnicity from one of six options and "ethnic/race minority status" was defined as "nonwhite/ Caucasian and/or Hispanic". AHI = apnea hypopnea index. BMI = body mass index. CRP= C-reactive protein. IL-6 = interleukin-6. PLMI = periodic limb movement index. TNF-α = tumor necrosis factor alpha.

Table 2.

Association between childhood and adolescence anthropometric characteristics and inflammatory biomarkers with apnea hypopnea index in adolescence

	Follow-up AHI		
	Univariate[a]	**Model 1[b]**	**Model 2[c]**
Baseline			
Height, cm	0.055 (0.393)	---	---
Weight, kg	0.104(0.107)	---	---
zBMI, z-score	0.064 (0.325)	---	---
BMI%, percentile	0.072 (0.267)	---	---
Neck circumference, cm	0.046 (0.496)	---	---
Waist circumference, cm	**0.203 (0.002)**	**0.157 (0.038)**	---
Waist circumference > 85%	**0.236 (<0.001)**	**0.227 (0.001)**	**0.191 (0.002)**
Hips circumference, cm	0.063 (0.329)	---	---
Follow-up			
Height, cm	0.044 (0.491)	---	---
Weight, kg	**0.160 (0.012)**	0.120(0.109)	---
zBMI, z-score	0.112(0.082)	---	---
BMI%, percentile	0.116(0.072)	---	---
Neck circumference, cm	0.107(0.097)	---	---
Waist circumference, cm	**0.150 (0.020)**	0.109(0.115)	---
Waist circumference ≥ 85%	0.023 (0.720)	---	---
Hips circumference, cm	0.048 (0.456)	---	---
Gynoid/whole ratio, %	−0.063 (0.349)	---	---
Android/whole ratio, %	**0.213 (0.001)**	**0.196 (0.003)**	**NS**
Subcutaneous tissue, cm^2	**0.136 (0.043)**	**0.235 (0.013)**	**NS**
Visceral tissue, cm^2	**0.318 (<0.001)**	**0.309 (<0.001)**	**0.249 (<0.001)**
CRP, mg/L	**0.231 (0.001)**	**0.221 (0.001)**	**0.163 (0.007)**
IL-6, pg/mL	**0.257 (<0.001)**	**0.243 (<0.001)**	**0.189 (0.002)**
TNF-α, pg/mL	−0.038 (0.587)	---	---
Leptin, ng/mL	0.019(0.785)	---	---
Adiponectin, μg/mL	0.096(0.161)	---	---

AHI = apnea hypopnea index. BMI = body mass index. CRP = C-reactive protein. IL-6 = interleukin-6. TNF-α = tumor necrosis factor alpha.

[a]Data are standardized beta coefficients (p-value) from univariate linear regression models.

[b]Data are standardized beta coefficients (p-value) from multivariable linear regression models adjusted for sex, race, adenotonsillectomy, and age and AHI at baseline (forced entry).

[c]Data are standardized beta coefficients (p-value) from a multivariable stepwise linear regression model of all significant factors (backward elimination) adjusted for sex, race, adenotonsillectomy, and age and AHI at baseline (forced entry). NS = not-significant, i.e., did not enter the stepwise model.

Bold values indicate statistical significance at $p \leq 0.05$.

Table 3.

Differences across groups with sleep disordered breathing in adolescence

	Follow-up SDB[a]				
	None (n=102)	**Snoring (n=68)**	**2<AHI<5 (n=57)**	**AHI>5 (n=15)**	**P**
Adenotonsillectomy, %	8.8%	8.8%	12.3%	13.3%	0.507
Baseline					
Age, years	8.4(1.5)	8.5(1.8)	8.7(1.7)	9.3(1.8)	**0.028**
AHI, events/hour	0.7 (0.8)	0.5 (0.6)	0.9(1.3)	0.7 (0.8)	0.310
Waist circumference, cm	59.2 (4.7)	60.2 (5.0)	60.8 (5.3)	61.0(6.5)	**0.037**
Follow-up					
Age, years	16.4 (2.0)	16.6 (2.3)	17.2 (2.2)	18.9(2.1)	**<0.001**
AHI, events/hour	0.8 (0.6)	1.0 (0.5)	3.0 (0.8)	15.0(22.1)	**<0.001**
Waist circumference, cm	71.6(6.7)	72.9 (5.5)	75.4 (8.6)	77.3 (7.4)	**0.001**
Gynoid/whole ratio, %	1.8(2.6)	1.9(2.7)	1.8(2.0)	1.8(2.5)	0.282
Android/whole ratio, %	5.4(1.0)	5.5 (0.9)	5.7(1.0)	5.9(1.1)	**0.038**
Subcutaneous tissue, cm^2	147.6 (83.5)	127.3 (80.9)	135.5 (94.2)	154.6 (94.2)	0.691
Visceral tissue, cm^2	36.1(15.1)	37.4(12.2)	40.4 (14.6)	51.1 (20.0)	**<0.001**
CRP, mg/L	0.6 (0.4)	0.5 (0.5)	0.8 (0.7)	1.3(0.6)	**<0.001**
IL-6, pg/mL	1.0(0.7)	1.1(1.0)	0.8 (0.7)	1.4(1.2)	0.234

[a]Data are mean (standard deviation) for continuous variable and percentage for categorical variables. Bold p-values are statistically significant at p-linear ≤ 0.05. AHI = apnea hypopnea index. CRP = C-reactive protein. IL-6 = interleukin-6. SDB = sleep disordered breathing.