Pediatric Obstructive Sleep-Disordered Breathing is Associated with Arterial Stiffness

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Research Article

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Abstract

Purpose

The association between obstructive sleep-disordered breathing (oSDB) and arterial stiffness, an independent predictor of cardiovascular outcomes, is not well established in children. This study compared cardiovascular parameters between healthy and oSDB children and aimed to identify predictors of arterial stiffness indices in children with oSDB.

Methods

Cross-sectional study realized in a tertiary hospital from June 2018 to January 2020. 48 children (3 to 10 years old) with clinical diagnosis of oSDB and indication for adenotonsillectomy and 24 controls were evaluated. Cardiovascular parameters were measured non-invasively by brachial artery oscillometry with a portable device. The main arterial stiffness indices assessed were augmentation index and pulse wave velocity, both derived from the aortic pulse wave. In the oSDB group, the questionnaires *Obstructive Sleep Apnea-18* and *Pediatric Quality of Life Inventory version 4.0* were applied.

Results

The oSDB group had higher values of reflection coefficient ($p = 0.044$) and augmentation index ($p = 0.003$) than the control group. Stepwise multiple regression analysis revealed that age, female sex, reflection coefficient and systolic volume were independent predictors of augmentation index. Higher pulse wave velocity values were associated with worse quality of life assessed by PedsQL questionnaire. There was no association with OSA-18. The vascular and hemodynamic parameters were similar in both groups.

Conclusion

Children with oSDB have increased augmentation index, an independent predictor of cardiovascular outcomes. The early identification of subclinical cardiovascular changes reinforces the importance of treating the disease, as well as changing lifestyle habits, to prevent complications in adulthood.

What Is Known

- The association between oSDB and cardiovascular risk in adults is well described in the literature.
- Children with oSDB, regardless of their weight or sex, have higher PWV values when compared to non-snoring children.

What Is New

- Children with oSDB have augmented arterial stiffness, evidenced by the increase in AIx@75, measured non-invasively by brachial artery oscillometry with a portable device.
- Low quality of life and therefore a high disease burden in children with oSDB may be a risk factor for arterial stiffness.

Introduction

Obstructive sleep-disordered breathing (oSDB) is a common disorder in childhood, interfering with the patient's physical, cognitive, emotional and social development.[1] This term is used when symptoms are present, but without definition of the severity of airway obstruction assessed by objective methods such as polysomnography (PSG). [2]

The association between oSDB and cardiovascular risk in adults is described in the literature.[3] Cicero et al. described that self-reported snoring and sleep apnea were considered main independent predictors associated with higher pulse wave velocity (PWV), the gold standard for measuring arterial stiffness, and that augmentation index (AIx), an indirect index of arterial stiffness and direct left ventricular afterload, was significantly higher in snorers with or without apnea than in non-snorers.[4] Thus, oSDB appears to be a modifiable risk factor for cardiovascular morbidity and mortality.[5]

Lately, the impacts of oSDB in children have received more attention. Studies have already shown that both isolated snoring and apneas are associated with worse quality of life, behavior, cognition and that children with oSDB have a two to three-fold increase in the use of health services.[6][7][8] Evidences of autonomic dysfunction have been reported, both during wake or sleep, as well as pressure changes and increased sympathetic activity in school-aged children and adolescents. [9]

To date, no publications are available in the literature describing arterial stiffness indices for children diagnosed with oSDB. This study aims to compare cardiovascular parameters between healthy children with oSDB and to identify predictors of arterial stiffness indices in children with oSDB.

Methods

Sample Characterization

This is a cross-sectional study from a tertiary hospital in Brazil from June 2018 to January 2020. Children aged between 3 and 10 years with diagnosis of oSDB and indication for adenotonsillectomy (T&A) were selected. The diagnosis and indication for treatment were based on the following symptoms, lasting at least 6 months: snoring, mouth breathing, noisy breathing, pauses in breathing during sleep and daytime symptoms as inattention, poor concentration, hyperactivity, or excessive sleepiness. No PSG was performed, in accordance with American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) practice guidelines.[10] Patients diagnosed with craniofacial dysmorphia, asthma, neuromuscular

diseases, congenital or acquired cardiac abnormalities, rheumatological diseases, acute or chronic liver diseases, renal failure and diabetes were excluded from the sample. Control group consisted of children considered healthy, matched by sex and age.

Forty-eight patients were compared with 24 children from a control group. The study was approved by the local Research Ethics Committee, under protocol number 08812019000005134, and the informed consent for parents and minors was obtained in all cases.

The sample size was calculated to test the difference between the means of augmentation index normalized to heart rate of 75 beats per minute (AIx@75) between cases and controls. At the significance level of 5% and minimum power of 80%, at least 48 cases and 24 controls were required.

Examination protocol

Tonsils 'hypertrophy was classified according to the Brodsky scale from 0 to 4. Adenoid hypertrophy was classified according to the percentage of adenoid occupation in the nasopharynx. Children were classified according to the body mass index (BMI) as underweight (percentile ≤ 3), eutrophic (percentiles 3-85), overweight (percentiles 85-97) and obese (percentile ≥ 97). Duration of symptoms and comorbidities were registered for all participants.

Quality of life

The following questionnaires were applied to evaluate quality of life in oSDB group: *Obstructive Sleep Apnea-18* (OSA-18) [11] and *Pediatric Quality of Life Inventory, version 4.0* (PedsQL 4.0) [12], both translated and validated into portuguese. The first assesses quality of life specifically related to oSDB and the second is a generic quality of life questionnaire for children.

Cardiovascular assessment

Cardiovascular parameters and arterial stiffness indices were collected non-invasively using the *Mobil-O-Graph®* device (IEM, Stolberg, Germany). This equipment incorporates the ARCSolver method (Austrian Institute of Technology), capable of reconstructing the aortic pulse wave from the brachial oscillometric pressure using a transfer function. This method obtains peripheral arterial pressure by a pressurized occlusion cuff, aiming complete interruption of the artery blood flow. Oscillations are perceived as the cuff is deflated from a pressure above peripheral systolic blood pressure (pSBD) to below peripheral diastolic blood pressure (pDBP). The registration of the central data is performed at the pDBP level for approximately 10 seconds, using a high fidelity pressure sensor.[13] The device performs measurements in triplicate and the average of the three acceptable measurements is considered for the final analysis of all evaluated parameters. To carry out this measure, children abstained from physical activity for at least 24 hours and from consuming caffeine and chocolate on the day of the exam.

The main arterial stiffness indices evaluated by the device were PWV and AIx@75. PWV is determined by means of a mathematical model, considering various parameters in the pulse wave and wave separation

analysis. In the absence of arterial stiffness, PWV is low, due to the distension of the arterial wall and damping of the pulse wave. AIx consists of the ratio between the augmentation pressure (AP) and the central pulse pressure (cPP) and is expressed as a percentage. AP is the difference between the first and the second systolic peaks (AP = P2-P1), which corresponds to the increase in central systolic blood pressure (cSBP) due to the reflection wave. Thus, the greater the reflection of the pulse wave, the greater will be the AP and the AIx. AIx@75 is the AIx normalized for the heart rate of 75 beats per minute (Figure 1).[14]

The cPP, difference between systolic and central diastolic blood pressure, as well as cSBP, are other indices of arterial stiffness. In addition, the equipment evaluates peripheral systolic blood pressure (pSBP), peripheral diastolic blood pressure (pDBP), peripheral pulse pressure (PP) and mean arterial pressure (MAP). Hemodynamic parameters such as systolic volume (SV), cardiac output (CO), total vascular resistance (TVR), cardiac index (IC) and heart rate (HR) were also assessed.

Statistical Analysis

Qualitative variables were presented as absolute and relative frequencies and quantitative variables as mean ± standard deviation. Quantitative variables were submitted to the Shapiro-Wilk normality test. The association between qualitative variables was assessed using the Chi-square test and binary logistic model. To compare quantitative variables between two groups, Student's t-tests for independent samples and the Wilcoxon Mann-Whitney test were used. The single-factor analysis of variance was used to evaluate the comparison of means between three or more groups and Pearson and Spearman's linear correlation coefficients were used to assess the correlation between two quantitative variables.

For PWV and Aix@75, a multiple linear regression model was constructed. Variables with $p < 0.20$ in the association analysis were included in a saturated model and, adopting the *stepwise* strategy, the final models were obtained with the significant variables and the age variable, regardless of significance, for effect control. The quality of the adjustment was assessed via adjusted R^2 and residue analysis. The analysis was performed using the R software version 4.0.2 and a significance level of 0.05 was considered.

Results

The sample consisted of 72 children, 56.9% of them male and with an average age of 5.40 ± 2.01 years. There were 24 in the control group and 48 in the oSDB group. The control and oSDB groups were similar in terms of gender, age, BMI, and height (Table 1).

Table 2 shows the peripheral and central vascular pressures, hemodynamic parameters, and arterial stiffness indices in the control and oSDB groups. The oSDB group had higher values of reflection coefficient (RC) ($p = 0.044$) and AIx@75 ($p = 0.003$) than the control group (Table 2). The other parameters were similar in both groups.

AIx@75 had an inverse relationship with age (r = -0.358, p = 0.013) and SV (r = -0.626, p <0.001). RC (r = 0.530, p <0.001) had a direct correlation with AIx@75. For the final model, the predictors os Aix@75 increase were age, female sex, RC and SV, the equation being represented by “AIx@75 = 3.525 + 8.35 (female) - 0.449 (age, years) - 0.5 (SV, ml) + 0.801 (RC)” (Table 3). PWV had an inverse relationship with the total score of the *PedsQLquestionnaire (*r= -0.319, p=0.042). The predictors of PWV were age, central diastolic blood pressure (cDBP), CO and AP: “PWV = 1.019 + 0.005 (age years) + 0.013 (cDBP, mmHg) + 0.394 (CO, ml/min) + 0.041 (AP, mmHg)” (Table 3). OSA-18 questionnaire, height of participants and size of tonsils did not correlate with parameters of arterial stiffness.

Discussion

This study demonstrated, for the first time, that children with oSDB have augmented arterial stiffness, evidenced by the increase in AIx@75, measured non-invasively by brachial artery oscillometry with a portable device. emale gender, age, SV, and RC were independent determinants of AIx@75 response in oSDB children. There was no difference in PWV between groups. However, it had an inverse relationship with the total score of the *PedsQLquestionnaire*. These data suggest that children with oSDB have subclinical changes in vascular parameters that could lead to the development of cardiovascular diseases in adulthood.

There are few validation studies that compare invasive and non-invasive measures of arterial stiffness in children. Shiraishi et al (2020) demonstrated that central pressure measures performed by *Mobil-o-graph*® in children and adolescents are accurate and promising for future studies and research.[15] Furthermore, there are already standardized values of arterial stiffness indices for children, which allow the evaluation of these indicators in this age group. [16][17] Other studies have described arterial stiffness are present in childhood and AIx@75 reference equations have been proposed for children in different health conditions. [17] Walter et al (2018) reported changes in arterial stiffness in children with oSDB through increased PWV. [18] Similarly, Montero Lopez et al (2019), described a positive correlation of PWV with BMI in a multicenter study involving children aged 9 to 10 years. [19]

In addition to the increased AIx@75 in children with oSDB, it was observed in our results that AIx@75 in females was 31.64% higher than in males. However, the difference was not significant. Despite this, the sex variable was introduced in the multiple regression model, as well as all other variables with p < 0.2. Ayer et al. (2010) described that healthy girls, assessed in the first decade of life, had higher AIx compared to boys, regardless of the individual's height or arterial diameter.[20] This change is also described in female adults.[21] As discussed by Ayer et al, this finding suggests that factors responsible for higher AIx in women in adulthood would already be determined in the first decade of life and, in part, unrelated to height. These authors also reported that such data could justify different cardiovascular responses in men and women in adulthood for the same disease. Thus, such a result would be expected in the sample of this study.

Hidvégi et al [22] described in healthy children that AIx@75 tends to decrease in both sexes with age, occurring at different times due to puberty. This phenomenon is explained by the short stature, which leads to an early return of the reflection wave. In the present study, data related to puberty were not evaluated. However, the influence of this factor would not be expected, since the average age of the children evaluated was 5 years, lower than the beginning of puberty. In addition, height was similar in both groups and higher levels of AIx@75 in the oSDB group could not be attributed to it.

The magnitude of the reflection wave is assessed by the RC, which is defined by the relationship between the amplitude of the reflection wave and the ejection wave. Thus, the concomitant increase in AIx@75 is expected since the greater the amplitude of the reflection wave, the greater the RC, the greater the AP and the greater the AIx@75. The last predictor of AIx@75 in children with oSDB is SV. Increase in SV reduces AIx@75. Similar results were described by Santos et al in healthy children.[23]

Obesity is an independent risk factor for cardiovascular morbidity.[24] In this study, 16.7% of the children were classified as overweight and 18.8% as obese in the oSDB group compared to 1.5% of overweight and no obese children in the control group. Walter et al showed that overweight and obese children with oSDB had higher PWV than normal weight children with oSDB, which suggests obesity as an exacerbation factor of arterial stiffness in this age group. [18] Obesity can aggravate the effects of oSDB because the macrophages present in adipose tissue are the target of the effects of intermittent hypoxemia, leading to an increase in inflammatory markers. The study *Icelandic Sleep Apnea Cohort* suggested that oSDB could result in a progressive inflammatory state, which would justify the mechanism of vascular damage and that such consequences could vary with the degree of obesity.[25] There were no differences in BMI between the oSDB and control groups in the hereby investigated cohort. Similarly to the existing literature, BMI correlated positively with the PWV arterial stiffness indices ($r= 0.359$, $p=0.012$) and cSBP.

Guilleminault et al (1976) were the first to describe children with oSDB and high blood pressure (BP). [1] Walter et al. (2018) were the first to describe that both during wakefulness and during sleep, children with oSDB, regardless of their weight or sex, had higher PWV values when compared to non-snoring children in the control group. [18] In contrast, our study revealed similar PWV between control and oSDB groups. However, it was observed that it correlated negatively with the social, physical, and total scores of the *PEDSQL 4.0questionnaire* in the oSDB group. These results suggest that a low quality of life and therefore a high disease burden in children with oSDB may be a risk factor for arterial stiffness. To the best of our knowledge, this study was the first to demonstrate an association between PWV and quality of life in children with oSDB. Tap et al. (2020) demonstrated an association between arterial stiffness and low quality of life in Dutch elderly people over 75 years old, regardless of age, blood pressure levels and comorbidities. [26] The authors suggested that the findings could be explained by poor physical or mental health. Other authors [27, 28] demonstrated a relationship between low quality of life and arterial stiffness. However, these studies were performed in an adult population with specific comorbidities.

Arterial stiffness is a predictor of cardiovascular diseases [29], and therefore its investigation is important. In a meta-analysis, Li et al described that a 10% increase in AIx in adults is related to an 1.18 relative risk of increased chance of cardiovascular events. [30] In order to evaluate the prognostic impact of increased AIx on the future cardiovascular risk in this sample, children would have to be followed up to adulthood and should not be treated for oSDB, which would be ethically objectionable. However, the hereby-presented observations indicate the importance of diagnosis and appropriate treatment of oSDB in children. It is well-known in the literature that treatment of apnea in the adult population leads to significant improvements in cardiovascular function, which includes a reduction in pulmonary artery pressure, MAP and endothelial dysfunction.[5] Changes in PWV are more marked in older individuals (50 years), suggesting that AIx might be a more sensitive marker of arterial aging in younger individuals, and PWV more sensitive in those over 50 years of age. [31]

The implications of treating oSDB in children and their cardiovascular outcomes are still poorly explored. Existing studies vary in terms of methods and evaluation of results. Since the main cause of oSDB in children is adenotonsillar hypertrophy, T&A would be the first line of treatment for this disease. [6] Although Apostolidou et al [7] and NG et al [8] have shown a decrease in diastolic blood pressure in children undergoing this surgical procedure, these authors have not been able to conclude about its medium and long term effects on the cardiovascular system. Furthermore, it is already discussed that surgery does not always lead to complete resolution of oSDB symptoms.[1] Bhattacharjee R et al., in a retrospective study, concluded that residual disease is present in a large proportion of children after T&A. [32] Comparably, Yu-Shu Huang and coworkers, in a prospective study, described that T&A leads to significant improvement in PSG findings, though generally with incomplete resolution and a worsening over time.[33] Thus, one must also question T&A´s role in resolving arterial stiffness, which would be the subject of a new study.

Study limitation

In adults, arterial stiffness is associated with both the presence and severity of oSDB. PSG is necessary to stratify the severity of oSDB.[2] AAO-HNS produced clinical guidelines or practice parameters regarding indications for PSG in children. [10] Currently in Brazil, PSG is not required for T&A indication since it is a costly and time-consuming test, and not all sleep laboratories evaluate children. Moreover, its use for scientific purposes is even more limited in our country. Thus, PSG was not performed in our sample. Another limitation of this study is its cross-sectional character, which prevents causal associations and reduces the generalizability of regression analyzes. Furthermore, it was carried out in a single center, which reduces the external validity of the data.

Conclusion

This study demonstrated that children with oSDB have arterial stiffness due to an increase in AIx@75. In addition, it was observed that there was a correlation between low quality of life and increased PWV in the oSDB group. The early identification of subclinical cardiovascular changes reinforces the importance

of treating the disease, as well as changing lifestyle habits, to prevent complications in adulthood. Further studies are needed to determine the precise impact of oSDB treatment on arterial stiffness indices.

Abbreviations

AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery

AIx@75: Augmentation index normalized to heart rate of 75 bpm

AP: Augmentation pressure

BMI: Body mass index

cDBP: central diastolic blood pressure

CI: Cardiac index

CO: Cardiac output

cPP: central pulse pressure

cSBP: central systolic blood pressure

HR: Heart rate

MAP: Mean arterial pressure

OSA-18: Obstructive Sleep Apnea-18 questionaire

oSDB: obstructive sleep-disordered breathing

pDBP: peripheral diastolic blood pressure

PedsQL: Pediatric Quality of Life Inventory, version 4.0

PPA: Pulse pressure amplification (PPp/PPc ratio)

pPP: peripheral pulse pressure

pSBP: peripheral systolic blood pressure

PSG: polysomnography

PWV - Pulse wave velocity

RC: Reflex coefficient

SV: Systolic volume

T&A : adenotonsillectomy

TVR: Total vascular resistance

Declarations

Funding

N/A

Conflicts of interest/Competing interests

N/A

Availability of data and material

All data is available in .pdf or .xls for appraisal.

Code availability

N/A

Authors' contributions

Rossi-Monteiro, EM: selected patients, conceived and outlined the study, coordinated and supervised data collection, analyzed and interpreted the data, drafted, edited and critically reviewed the manuscript for important intellectual content.

Sefair, LR; Lima, MC; Nascimento, MFL: contributed to the data collection and reviewed the manuscript for important intellectual content.

Rodrigues-Machado, MG: conceived and designed the study, analyzed and interpreted the data, drafted, edited and critically revised the manuscript for important intellectual content.

Mendes-Pinto, D: revised the manuscript for important intellectual content.

Anschuetz, L: revised the manuscript for important intellectual content.

All authors read and approved the final version of the manuscript.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration

and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Faculdade Ciências Médicas de Minas Gerais under the protocol number 08812019000005134.

Consent to participate

Informed assent was obtained from all minors' participants included in the study.

Written informed consent was obtained from the parents or legal guardians.

Consent for publication

All parents or legal guardians have signed informed consent regarding publishing data about their children.

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Tables

Table 1

Socio-demographic, anthropometric, clinical variables, and quality of life for control and oSDB groups

Variables	Control (n = 24)	oSDB (n = 48)	P-value
Sociodemographic and anthropometric			
Sex			0.933[Q]
Male	13 (54.2%)	28 (58.3%)	
Female	11 (45.8%)	20 (41.7%)	
Age (y)	5.71 ± 2.03 (5)	5.25 ± 2.01 (5)	0.311[W]
BMI	16.06 ± 1.71 (15.96)	16.50 ± 3.17 (16)	0.451[T]
Low weight	3 (12.5%)	9 (18.8%)	
Normal weight	18 (75%)	22 (45.8%)	
Overweight	3 (1.5%)	8 (16.7%)	
Obese	-	9 (18.8%)	
Height (m)	1.16 ± 0.15 (1.13)	1.14 ± 0.15 (1.10)	0.6116
Quality of Life			
PesdsQL 4.0 Total Scale	-	74.51 ± 14.95 (75)	-
Emotional Functioning	-	57.00 ± 20.19 (55)	-
Social Functioning	-	85.00 ± 14.95 (90)	-
School Functioning	-	73.76 ± 24.93 (83.3)	-

Data is presented as mean ± standard deviation (median). oSDB: obstructive sleep-disordered breathing; BMI: Body mass index; PedsQL: Pediatric Quality of Life Inventory, version 4.0; OSA-18: Obstructive Sleep Apnea-18 questionaire;(): median; [Q] chi squared test, [W] Wilcoxon Mann-Whitney test, [T] T-Student t-test for independent samples, [L] binary logistic model.

Variables	Control (n = 24)	oSDB (n = 48)	P-value
Psychosocial Functioning	-	71.77 ± 14.70 (75)	-
Physical Functioning	-	79.65 ± 18.70 (81.3)	
OSA-18 Scale (n = 40)	-	68.17 ± 21.57 (67)	-
OSA-18 Category (n = 41)			-
Mild	-	14 (34.1%)	
Moderate	-	17 (41.5%)	
Severe	-	10 (24.4%)	
Clinical			
Adenoid Size (%)	-	75.83 ± 15.41 (80)	-
Tonsils Size (Brodsky)	-	2.69 ± 0.80 (3)	-

Data is presented as mean ± standard deviation (median). oSDB: obstructive sleep-disordered breathing; BMI: Body mass index; PedsQL: Pediatric Quality of Life Inventory, version 4.0; OSA-18: Obstructive Sleep Apnea-18 questionaire;(): median; [Q] chi squared test, [W] Wilcoxon Mann-Whitney test, [T] T-Student t-test for independent samples, [L] binary logistic model.

Table 2
Mobil-o-Graph variables classified by group

Variables	Control (n = 24)	oSDB (n = 48)	P-value
Peripheral Blood Pressure (mmHg)			
pSBP	101.60 ± 6.11 (100.5)	103.92 ± 10.16 (103)	0.232[T]
pDBP	58.38 ± 7.70 (58)	58.23 ± 7.05 (58.2)	0.938[T]
MAP	78.16 ± 6.70 (78.7)	79.20 ± 7.36 (78.7)	0.550[T]
pPP	43.52 ± 5.01 (43.8)	45.68 ± 8.80 (44)	0.190[T]
Central Blood Pressure (mmHg)			
cSBP	89.67 ± 6.49 (89)	91.16 ± 8.26 (90.7)	0.407[T]
cDBP	60.51 ± 7.51 (60.3)	60.25 ± 7.10 (60)	0.887[T]
cPP	29.32 ± 3.70 (29.2)	30.93 ± 6.14 (30.2)	0.171[T]
PPA	1.50 ± 0.11 (1.50)	1.48 ± 0.12 (1.50)	0.575[T]
Hemodynamic Parameters			
SV (ml)	45.39 ± 7.56 (44.1)	43.94 ± 7.96 (43.4)	0.496[W]
CO (ml/min)	4.14 ± 0.52 (4)	4.16 ± 0.61 (4.1)	0.858[W]
TVR (s*mm Hg/mL)	1.17 ± 0.13 (1.17)	1.16 ± 0.10 (1.14)	0.445[W]
IC (L/min/m^2)	5.06 ± 1.21 (5.1)	5.19 ± 1.08 (5)	0.652[T]
HR (bpm)	90.47 ± 13.20 (90.5)	96.08 ± 12.31 (96)	0.089[T]
Stiffness Parameters			
AP (mmHg)	6.49 ± 1.96 (6.3)	7.96 ± 3.84 (7.3)	0.175[W]

Data is presented as mean ± standard deviation (median). oSDB: Obstructive sleep-disordered breathing; pSBP: peripheral systolic blood pressure; pDBP: peripheral diastolic blood pressure; MAP: Mean arterial pressure; pPP: peripheral pulse pressure; cSBP: central systolic blood pressure; cDBP: central diastolic blood pressure; cPP: central pulse pressure; PPA: Pulse pressure amplification (PPp/PPc ratio); SV: Systolic volume; CO: Cardiac output; TVR: Total vascular resistance; CI: Cardiac index; HR: Heart rate; AP: Augmentation pressure; RC: Reflex coefficient; AIx@75: Augmentation index normalized to heart rate of 75 bpm; PWV - Pulse wave velocity; [W] Wilcoxon Mann-Whitney test, [T] T-Student t-test for independent samples, [L] binary logistic model.

Variables	Control (n = 24)	oSDB (n = 48)	P-value
CR	62.34 ± 4.99 (62.7)	65.18 ± 6.44 (65)	0.044[T]
AIx@75 (%)	29.56 ± 7.09 (29.4)	36.54 ± 11.82 (36.3)	0.003[T]
PWV (m/sec)	4.22 ± 0.21 (4.2)	4.26 ± 0.33 (4.2)	0.606[T]

Data is presented as mean ± standard deviation (median). oSDB: Obstructive sleep-disordered breathing; pSBP: peripheral systolic blood pressure; pDBP: peripheral diastolic blood pressure; MAP: Mean arterial pressure; pPP: peripheral pulse pressure; cSBP: central systolic blood pressure; cDBP: central diastolic blood pressure; cPP: central pulse pressure; PPA: Pulse pressure amplification (PPp/PPc ratio); SV: Systolic volume; CO: Cardiac output; TVR: Total vascular resistance; CI: Cardiac index; HR: Heart rate; AP: Augmentation pressure; RC: Reflex coefficient; AIx@75: Augmentation index normalized to heart rate of 75 bpm; PWV - Pulse wave velocity; [W] Wilcoxon Mann-Whitney test, [T] T-Student t-test for independent samples, [L] binary logistic model.

Table 3

Stepwise multiple regression analysis for arterial stiffness indices in oSDB group

Variables	AIx@75	PWV
Constant	3.525 (p = 0.810)	1.019 (p < 0.001)
Female Sex	8.350 (p < 0.001)	-
Age	-0.469 (p = 0.425)	0.005 (p < 0.001)
Peds Total	-	-
cDBP	-	0.013 (p < 0.001)
cPP	-	-
CO	-	0.394 (p < 0.001)
AP	-	0.041 (p < 0.001)
SV	-0.500 (p < 0.001)	-
RC	0.801 (p < 0.001)	-
Adjusted R^2	69.00%	84.02%

oSBP: obstructive sleep-disordered breathing; AIx@75: augmentation index normalized to heart rate of 75 bpm; PWV: pulse wave velocity; Peds Total: Pediatric Quality of Life Inventory, version 4.0, Total Scale; cDBP: central diastolic blood pressure; cPP: central pulse pressure; CO: cardiac output; AP: augmentation pressure; SV: systolic volume; RC: reflex coefficient.

Figures

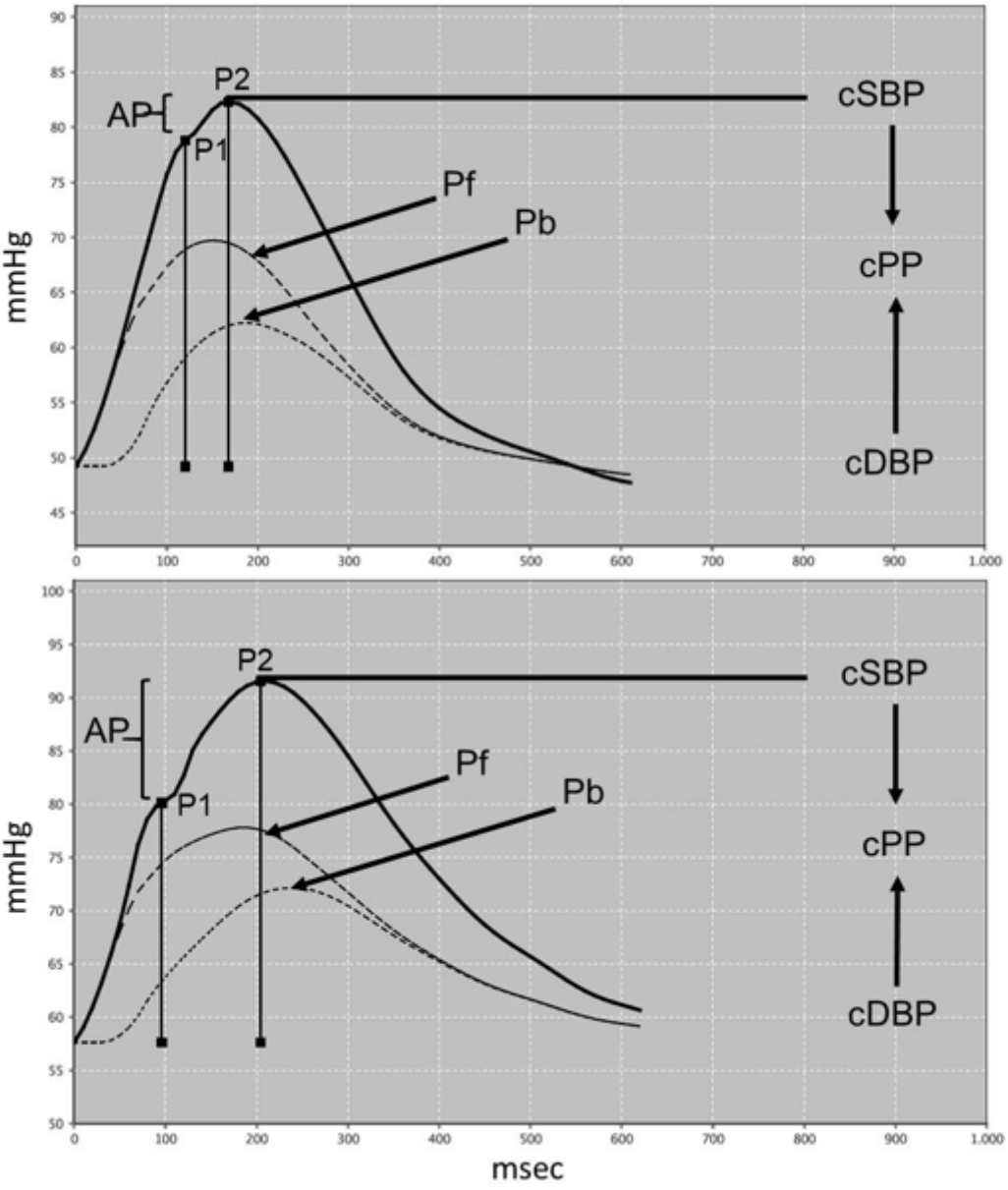

Figure 1

Pulse waves from the aortic arteries in (A) a child from control group and (B) a child from oSDB group. The forward wave (Pf) propagates in the arterial system after each systole and forms the first systolic peak (P1). Due to the increased resistance, the reflection wave (Pb) is transmitted in a retrograde way, increasing cSBP (P2). Pb/Pf ratio represents the magnitude of reflection wave. The difference between P2 and P1 is known as augmentation pressure (AP). Augmentation index represents the relationship of AP to central pulse pressure (cPP) expressed as a percentage (AIx = [P2 - P1]/PPc x 100]). cSBP: central systolic blood pressure; cDBP: central diastolic blood pressure; msec: millisecond; mmHg: blood pressure by mercury millimeters.