The Effect of Obesity on Asthma: Analysis of Pulmonary Function Using Impulse Oscillometry in School-age Children

Zeynep Güleç Köksal, Pınar Uysal

Aydın Adnan Menderes University School of Medicine, Department of Pediatric Allergy and Immunology, Aydın, Turkey

10.5222/TP.2020.70288

Cite as: Güleç Köksal Z, Uysal P. The effect of obesity on asthma: Analysis of pulmonary function using impulse oscillometry in school-age children. Trends in Pediatrics 2020;1(2):31-8.

Received: 16 November 2020
Accepted: 23 November 2020
Publication date: 31 December 2020

Keywords: Asthma, impulse oscillometry, pulmonary function, obesity, children

Zeynep Güleç Köksal
Aydın Adnan Menderes University School of Medicine,
Department of Pediatric Allergy and Immunology
09010 Aydın - Turkey
ORCID: 0000-0001-9464-4605
zynp.glc@hotmail.com

P. Uysal 0000-0003-0288-608X

ABSTRACT

Objective: *Studies investigating the pulmonary function of school-age obese asthmatics are rare. The purpose of this study was to compare lung functions in school-age obese asthmatics and non-obese asthmatics.*
Methods: *Ninety-two children were assigned to groups of obese asthmatics (Group OA, n=43) and non-obese asthmatics (Group A, n=49) baseline impulse oscillometry test was performed to measure pulmonary functions.*
Results: *Baseline percent predicted value of R20 (p=0.025), R5-20 (p=0.040), and Fres (p=0.018) were significantly increased in obese asthmatics than non-obese asthmatics. AX was also higher in obese asthmatics compared to non-obese asthmatics, however, the intergroup difference was insignificant (p=0.787). Percent predicted value of R5 (p=0.007) and R10 (p=0.017) were higher in atopic than non-atopic obese asthmatics. Percent predicted value of R5 was higher in exercise-intolerant than exercise-tolerant non-obese asthmatics (p=0.045). Additionally, R10 was higher in non-obese asthmatics who were exposed to household mold when compared with those without exposure to household mold (p=0.045). The z scores of BMI or weight were not correlated with any one of the IOS parameters (p>0.05).*
Conclusion: *Main bronchial and peripheral airway resistance was higher in school-age obese asthmatics compared to non-obese asthmatics. Peripheral airway resistance was higher in atopic obese asthmatics as well as well as asthmatic children with exercise intolerance and household mould exposure.*

INTRODUCTION

Asthma and obesity are the two most common chronic diseases in children with increasing prevalence worldwide.[1,2] The parallel increase in the prevalence of pediatric obesity and asthma suggests a possible association between them both in children and adults.[3-6] Although, obesity-related asthma is thought to be a separate entity[7], the underlying mechanisms in children have not been fully explained. Several studies are supporting that the risk of developing asthma symptoms increases as the body mass index (BMI) increases[8-10] and asthma treatment responses can be affected by BMI.[10,11] Moreover, in the presence of obesity, the severity of asthma, the risk of asthma exacerbation, rates of hospitalization, and drug use increase.[8-9]

Spirometry is the most widely used method of analysis worldwide to evaluate pulmonary functions. It is quite difficult to apply this technique appropriately in young children because it requires high cooperation of the patient.[12] Obesity is often associated with respiratory symptoms, but many patients also have normal spirometry results. A recent meta-analysis and some large-scale studies evaluated the differences between BMI and spirometry parameters, emphasizing that obese asthmatics have different

pulmonary function dynamics.[13,14]

Spirometry is a very useful technique for measuring functions of the larger airways, but insufficient for reflecting airflow through smaller airways. In contrast, impulse oscillometry (IOS) can provide a rapid and reliable assessment of airway resistance and reactance.[15,16] It is a new and alternative technique for evaluating pulmonary function tests in pediatric patients because it is an effort-independent method and requires minimal patient cooperation. It also helps in measuring airway resistance, determining chest wall reactance, and discriminating between central and peripheral airway functions.[17,18]

Some studies have used IOS to measure pulmonary functions in asthma, but there are not enough studies evaluating pulmonary functions of children with obesity co-existing asthma.[19-21] Therefore, the purpose of this study was to assess the pulmonary function using IOS in school-age obese asthmatics and to compare it with that of non-obese asthmatics.

MATERIALS AND METHODS

Study population

This retrospective cohort study was conducted between January 2020 and March 2020 at the tertiary referral hospital pediatric allergy and immunology clinic. Ninety-two children aged between 4 and 10 were included in the study. Participants did not have accompanying respiratory tract infections and all were receiving regular inhaled steroid therapy for at least three months. Children were assigned to two groups for IOS comparison: obese asthmatics (Group OA, n=43) and non-obese asthmatics (Group A, n=49).

Definitions:

Asthma: Definition of asthma was based on the Global Initiative for Asthma (GINA) guideline criteria: paroxysmal cough, wheezing, breathlessness, or chest tightness with either an increase in FEV1 of at least 12% or 200 mL after salbutamol administration or significant airway hyperresponsiveness.[22]

Obesity: Obesity was determined based on gender and age-specific cut-off values of BMI recommended by the International Obesity Task Force.[23] BMI was calculated using the formula weight (kg)/height^2 (m). The z scores for BMI were calculated using the Turkish Children Growth Reference Centiles.[24] The zBMI cut-off value for obesity was 1.90 kg/m^2 for girls and 1.84 kg/m^2 for boys (corresponding to BMI >30 kg/m^2 in young adults).

Atopy: Atopy was defined as a positive test result either by allergen-specific immunoglobulin E (sIgE) or skin prick test (SPT). Specific IgE value to common aeroallergens (Phadiotop) was defined as a positive value when it was above 0.35. Skin prick test positivity was defined as the presence of cutaneous reaction against common allergen(s) including Aspergillus fumigatus, *Alternaria alterna*, dust mite (*Dermatophagoides pteronyssinus* or *Dermatophagoides farinae*), cockroach mix, and grass mix.

Exclusion criteria:

Patients with a past and present history of chronic respiratory diseases other than asthma, chronic cardiac and neuromuscular disease, low birth weight/preterm birth/neonatal mechanical ventilation, malignancy, immune deficiencies, connective tissue disease, acute respiratory disease in the previous four weeks, recent exacerbation of asthma, oral steroid use were excluded from the study.

Study design:

Patients' demographic characteristics, medical histories, clinical symptoms, physical examination findings, and laboratory parameters were recorded using a standard questionnaire investigating age, gender, personal or parental history of atopy, and environmental factors. Besides, allergen sIgE levels, SPT, and IOS measurement results were scanned from medical records.

All pulmonary function tests were performed in the respiratory laboratory of Pediatric Allergy and Immunology Department. The children were requested not to use short-acting beta-agonists for 8 hours and antihistamines or anti-leukotriene medications for 72 hours before pulmonary function testing.[25]

At least three acceptable IOS measurements were

taken by an experienced nurse, evaluating whether the IOS was appropriate and artificial for the entire duration of 30-second measurement.

Pulmonary Function Tests

Impulse oscillometry

A Jaeger MasterScreen IOS system (CareFusion, Yorba Linda, CA, USA) was used to measure the input impedance of the respiratory system. This procedure was performed in line with the American Thoracic Society/European Respiratory Society guidelines.[26] The main parameters included resistance (R5, R20), reactance (X5, X20), the frequency dependence of resistance calculated as the difference between resistance at 5 and 20 Hz (R5-R20, resistance at 5 Hz minus resistance at 20 Hz), resonant frequency (Fres), and area under the reactance curve (AX). Higher frequencies of R (~20Hz), reflecting the larger airways, were regarded as resistance in central airways. Lower frequencies of R (~5 Hz) provided information about the integrity of (smaller and larger) airways. Peripheral (smaller) airway resistance was defined as R5-R20.[26-28] Acceptable variability was 15%.[26] The coherence threshold was set to ≥0.6 at 5 Hz, and ≥0.8 at 20 Hz. The results for R5, R10, R20 were expressed as percent predicted values, and R5-20, AX, and Fres were expressed as crude values due to the lack of references. Baseline airway resistance (Rrs) and reactance (Xrs) at 5Hz and 20 Hz, Fres, and AX were evaluated.

Ethics

The study was approved by the local Research Ethics Committee (2020/213).

Statistical Analysis

SPSS version 22.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. For the estimates, significance was set at 5%, with a power of 80%, and 28 participants were considered sufficient for each group. Normality was assessed using the Kolmogorov- Smirnov test and descriptive statistics. Categorical variables were expressed as the number of cases and percentages. Continuous variables were expressed as mean values and standard deviations or median values and interquartile ranges (IQR-25 and 75 quartiles) depending on whether they were normally distributed. Nonparametric or parametric tests were performed accordingly. Comparisons of qualitative data were performed using the chi-square test, while comparisons of quantitative variables between non-obese and obese asthmatics were performed using either the Student t-test or the Mann- Whitney U test. Alpha value was set at <0.05 for all tests.

RESULTS

Ninety-two children were initially included and all of them completed the study [(49 boys (53.8%)].

A comparison of demographic data between the Group A (n=49) and Group OA (n=43) is presented in Table 1. No difference was observed between the two groups in terms of age, gender, height, history of personal, and parental atopy, co-morbid allergic or chronic diseases, exposure to environmental factors, and atopy [sIgE or SPT positivity] (p>0.05). The weight and BMI were higher in obese asthmatics than non-obese asthmatics (p<0.001 and p=0.047, respectively).

Baseline percent predicted R20 (p=0.025), R5-20 (p=0.040), and Fres (p=0.018) were significantly increased in obese asthmatics than non-obese asthmatics. AX was also increased in obese asthmatics than non-obese asthmatics, however, intergroup difference was insignificant (p=0.787) (Table 2). However, there were no differences between genders in terms of age, zBMI score, or IOS parameters (p>0.05) (Data not shown).

Percent predicted value of R5 (p=0.007) and R10 (p=0.017) were higher in atopic than non-atopic obese asthmatics. Percent predicted value of R5 was higher in exercise-intolerant than exercise-tolerant non-obese asthmatics (p=0.045). Additionally, R10 was higher in non-obese asthmatics with household mold exposure than those without (p=0.045) (Data not shown).

Correlation analysis between age and IOS parameters

The z scores of BMI or weight were not correlated with any one of the IOS parameters (p>0.05).

Age was positively correlated with percent predicted

Table 1. Comparison of demographic characteristics between the A group and OA group

Variable	A group (n=50)	OA group (n=40)	p value
Age, (years)	7 (5-9)	7 (5-10)	0.259
Gender, (% male)	24 (49%)	25 (59.5%)	0.314
Height, (z score)	0.11 (-0.51-1.07)	1.05 (0.05-1.68)	0.111
Weight, (z score)	0.16 (-0.65- 1.09)	2.37 (2.0-3.02)	<0.001
BMI, (z score)	-0.01 (-0.60-0.87)	2.04 (2.0-2.55)	0.047
Personal atopy history, (n, %)	18 (36.7%)	11 (26.2%)	0.282
Parental atopy history, (n, %)	24 (50%)	13 (37.1%)	0.245
Comorbidities			
Atopic diseases	30 (61.2%)	18 (43.9%)	0.101
Other chronic diseases	3 (6.1%)	5 (11.9%)	0.463
Exposure to environmental factors, (n, %)			
Passive smoking	20 (41.7%)	17 (47.2%)	0.612
Household smoke	17 (35.4%)	12 (33.3%)	0.842
Pet	4 (8.5%)	7 (19.4%)	0.196
Household mould	7 (14.6%)	8 (22.2%)	0.366
Allergy test positivity, (n, %)			0.282
Allergen specific IgE	10 (20.4%)	10 (23.8%)	0.339
Skin prick test	15 (30.6%)	9 (21.4%)	0.329

Abbreviations: *A group: asthma group, BMI: body mass index, IQR: interquartile range, OA group: obese asthma group, n: number, %: percentage*

Table 2. Comparison of impulse oscillometry parameters between the A group and OA group

	A group (n=50)	OA group (n=40)	p value
R5, (%)	104.79±21.95	104.16±17.98	0.883
R10, (%)	104 (92-115)	103.5 (92.5-114.25)	0.796
R20, (%)	107.26±17.62	110.04±20.31	**0.025**
R5-20, (kPa/L)	28.34±18.39	36.85±20.64	**0.040**
X5, (%)	82.85±35.10	79.83±36.19	0.687
X10, (%)	133.18±76.92	125.26±107.0	0.683
X20, (%)	-101.85±153.75	-71.24±199.88	0.412
Fres (Hz)	-135.10±33.94	119.45±27.11	**0.018**
AX (kPa/L)	1.56 (0.72-3.20)	1.90 (0.76-2.50)	0.787

Abbreviations: *A Group: asthma group, Hz: Hertz, kPa: kilopascal, L: liter, OA Group: obese asthma group, n=number, %: percent predictive value*

value of R20 (r=0.383, p=0.007) and X20 (r=0.418, p=0.003) but negatively correlated with R5-20 (r= -0.320, p=0.025) and Fres (r= - 0.420, p=0.003) in non-obese asthmatics. Similarly, age was positively correlated with percent predicted value of R20 (r=0.559, p<0.001) and X20 (r=0.451, p=0.003) but negatively correlated with R5-20 (r= -0.471, p=0.002) and Fres (r= - 0.566, p<0.001) in obese-asthmatics.

DISCUSSION

There are a few number of studies investigating the respiratory functions of school-age obese asthmatics in the literature. In this study, we assessed baseline airway resistance with reactance in school-age obese asthmatics and compared the data obtained with those for non-obese asthmatics.

The main finding of the present study was that school-age obese asthmatics exhibited higher airway resistance than non-obese asthmatics. An increase in airway resistance was determined in both central and peripheral airways. Thus, we speculated that persistent peripheral airway may be a result of low functional residual capacity and alveolar collapse due to the mass effect of fat in obesity.

Although obesity is known to affect pulmonary function, study results remain controversial for children.[29,30] Previous studies reported that BMI disproportionately impacts lung volumes and airflow among children.[31,32] Mass load of obesity can increase abdominal pressure and decrease the recoil capacity of the chest wall and may contribute to distal airway closure and reduction in lung volume.[33] The increased work of breathing and lower functional residual lung capacity may also be other possible causes.[34] Besides the mechanical effects, fat mass may negatively affect respiratory dynamics by mediating a low-grade chronic inflammation and obesity-related inflammatory mediators might exacerbate chronic airway inflammation.[35] Other possible environmental factors are sedentary lifestyle, high-calorie diet intake and low antioxidant consumption.[36] Some studies have reported that obese patients have higher airway resistance but no airway obstruction which is compatible with our results.[37] However, more research is needed, particularly considering the mechanisms underlying the relationship between asthma and obesity.

In literature, few studies have investigated pulmonary functions using IOS in children with obesity or obesity and asthma, and the findings are inconclusive. In one prospective cross-sectional study, Assumpçao et al. investigated IOS parameters among 81 children aged six to 14 years, 21 overweight, 30 obese, and 30 healthy controls. Percentage predicted values of impedance (Z5), resistance (R5), Fres, and AX representing airway obstruction were significantly higher in obese children than in the healthy controls.[38] Kalhoff et al. evaluated pulmonary functions of 518 pre-school children using IOS. R5 and X5 were mildly elevated in obese children compared to IOS reference values, but IOS values were not associated with BMI.[39] Ekström et al. reported that persistent overweight and obesity were associated with small airway obstruction with higher R5–20 and AX.[40] In another prospective study, pulmonary functions of 99 children hospitalized for bronchiolitis before the age of six months were evaluated using IOS at six years of age. Any significant differences were not observed in responses to exercise or to bronchodilators between currently obese or overweight children and normal-weight children. However, seven obese children had higher post-BD impedance in the airways and higher R5 values compared to normal-weight children.[19]

In the present study, entire airway resistance (increased R5 and R10) was found to be higher in obese asthmatics with atopic sensitivity than that without atopic sensitivity. Similarly, high airway resistance was found in those with mold allergen sensitivity (increased R10) and those with exercise intolerance (increased R5). We speculate that atopy may modify pulmonary functions by increasing airway inflammation that results in airway hyperresponsiveness and remodeling. In this regard, it comes to mind that some obesity-related mechanisms might potentiate deterioration of pulmonary function. Supporting our findings, in previous studies, higher FeNO levels reflecting higher eosinophilic airway inflammation were measured in subjects with obesity.[41]

Besides, low-level chronic inflammation caused by obesity is associated with increased leptin levels.[42] Leptin acts with Th1 cell differentiation, TNF-a, IFN-gamma, and IL-6 increase.[43] Therefore, chronic low-grade inflammation related to obesity may potentiate the effect of atopy on the deterioration of pulmonary functions in obese asthmatics more severely than that of non-obese asthmatics.

Although airway resistance was found to be higher in

obese asthmatics, there was no correlation between BMI and IOS parameters. Some studies presence of any relationship between pulmonary functions and BMI.[30,44] No effect of BMI on airway hyprereactivity was reported in a study conducted in more than 1000 children with mild to moderate asthma who were followed up to adulthood in the USA and Canada in Childhood Asthma Management Program (CAMP study).[45] Similarly, a prospective birth cohort study of more than 1000 children from New Zealand found no effect of BMI on AHR.[46] However, these studies were carried out using spirometry and there is no large-scale population study using the IOS method. Therefore, new studies are needed on this subject.

The particular strengths of the present study were that pulmonary functions and airway inflammation were examined using noninvasive methods under observation by the same highly experienced nurse and physician in all cases. All patients were examined by pediatric allergy and endocrine specialists. Treatment-naive children were included in the study to prevent potential drug interaction. Pulmonary function tests were performed at the same time of the day to eliminate the effects of potential diurnal variation.

There were also some limitations to this study. BMI is not the gold standard in assessing body composition, which is more indicative of body size than fat mass and does not distinguish fat mass from lean mass. The findings of this study should be interpreted with caution since they cannot be used to infer causality between obesity and asthma due to its cross-sectional design.

In conclusion, our findings have important implications for the interpretation of respiratory functions in school-age obese asthmatics. Obese asthmatics had higher airway resistance and measurements of pulmonary function using IOS appear to be more useful for an early understanding of the impact of obesity on lung functions of children with asthma. Our findings now need to be replicated in longitudinal studies of childhood obesity and asthma to shed further light on the complex interactions between the two entities.

Acknowledgments: The authors are indebted to the intern doctors Gozde Uykaz and Kenan Yoruk for the collection of analysis data.

Ethics Committee Approval: Local Ethical Committee at Aydin Adnan Menderes University (2020/213).
Conflict of Interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
Funding: The authors received no financial support for the research, authorship, and/or publication of this article.
Informed Consent: Parents of the patient provided informed consent to publish the report.

REFERENCES

1. Pearce N, Aït-Khaled N, Beasley R, et al. Worldwide trends in the prevalence of asthma symptoms: Phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax. 2007;62(9):757-65. https://doi.org/10.1136/thx.2006.070169
2. Di Cesare M, Sorić M, Bovet P, et al. The epidemiological burden of obesity in childhood: A worldwide epidemic requiring urgent action. BMC Med. 2019;17(1):1-20. https://doi.org/10.1186/s12916-019-1449-8
3. Castro-Rodríguez JA, Holberg CJ, Morgan WJ, Wright AL, Martinez FD. Increased incidence of asthmalike symptoms in girls who become overweight or obese during the school years. Am J Respir Crit Care Med. 2001;163(6):1344-9. https://doi.org/10.1164/ajrccm.163.6.2006140
4. Gilliland FD, Berhane K, Islam T, et al. Obesity and the risk of newly diagnosed asthma in school-age children. Am J Epidemiol. 2003;158(5):406-15. https://doi.org/10.1093/aje/kwg175
5. Cottrell L, Neal WA, Ice C, Perez MK, Piedimonte G. Metabolic abnormalities in children with asthma. Am J Respir Crit Care Med. 2011;183(4):441-8. https://doi.org/10.1164/rccm.201004-0603OC
6. Mitchell EA, Beasley R, Björkstén B, Crane J, García-Marcos L, Keil U. The association between BMI, vigorous physical activity and television viewing and the risk of symptoms of asthma, rhinoconjunctivitis and eczema in children and adolescents: ISAAC Phase Three. Clin Exp Allergy. 2013;43(1):73-84. https://doi.org/10.1111/cea.12024
7. Dixon AE, Holguin F, Sood A, et al. An official American thoracic society workshop report: Obesity and asthma. Proc Am Thorac Soc. 2010;7(5):325-35. https://doi.org/10.1513/pats.200903-013ST
8. Chen YC, Dong GH, Lin KC, Lee YL. Gender difference of childhood overweight and obesity in predicting the risk of incident asthma: A systematic review and meta-analysis. Obes Rev. 2013;14(3):222-31. https://doi.org/10.1111/j.1467-789X.2012.01055.x
9. Egan KB, Ettinger AS, Bracken MB. Childhood body mass index and subsequent physician-diagnosed asthma: A systematic review and meta-analysis of

prospective cohort studies. BMC Pediatr. 2013;13:121. https://doi.org/10.1186/1471-2431-13-121
10. Novosad S, Khan S, Wolfe B, Khan A. Role of Obesity in Asthma Control, the Obesity-Asthma Phenotype. J Allergy. 2013;2013:1-9. https://doi.org/10.1155/2013/538642
11. Forte GC, Grutcki DM, Menegotto SM, Pereira RP, Dalcin PDTR. Prevalence of obesity in asthma and its relations with asthma severity and control. Rev Assoc Med Bras. 2013;59(6):594-9. https://doi.org/10.1016/j.ramb.2013.06.015
12. Kaminsky DA. What does airway resistance tell us about lung function? Respir Care. 2012;57(1):85-99. https://doi.org/10.4187/respcare.01411
13. Forno E, Han YY, Mullen J, Celedón JC. Overweight, Obesity, and Lung Function in Children and Adults-A Meta-analysis. J Allergy Clin Immunol Pract. 2018;6(2):570-81.e10. https://doi.org/10.1016/j.jaip.2017.07.010
14. Han YY, Forno E, Celedón JC. Adiposity, fractional exhaled nitric oxide, and asthma in U.S. Children. Am J Respir Crit Care Med. 2014;190(1):32-9. https://doi.org/10.1164/rccm.201403-0565OC
15. Oppenheimer BW, MacHt R, Goldring RM, Stabile A, Berger KI, Parikh M. Distal airway dysfunction in obese subjects corrects after bariatric surgery. Surg Obes Relat Dis. 2012;8(5):582-9. https://doi.org/10.1016/j.soard.2011.08.004
16. Zerah F, Harf A, Perlemuter L, Lorino H, Lorino AM, Atlan G. Effects of obesity on respiratory resistance. Chest. 1993;103(5):1470-6. https://doi.org/10.1378/chest.103.5.1470
17. Komarow HD, Myles IA, Uzzaman A, Metcalfe DD. Impulse oscillometry in the evaluation of diseases of the airways in children. Ann Allergy, Asthma Immunol. 2011;106(3):191-9. https://doi.org/10.1016/j.anai.2010.11.011
18. Song TW, Kim KW, Kim ES, Park JW, Sohn MH, Kim KE. Utility of impulse oscillometry in young children with asthma. Pediatr Allergy Immunol. 2008;19(8):763-8. https://doi.org/10.1111/j.1399-3038.2008.00734.x
19. Lauhkonen E, Koponen P, Nuolivirta K, et al. Obesity and bronchial obstruction in impulse oscillometry at age 5-7 years in a prospective post-bronchiolitis cohort. Pediatr Pulmonol. 2015;50(9):908-14. https://doi.org/10.1002/ppul.23085
20. De Winter-De Groot KM, Van Der Ent CK, Prins I, Tersmette JM, Uiterwaal CSPM. Exhaled nitric oxide: The missing link between asthma and obesity? J Allergy Clin Immunol. 2005;115(2):419-20. https://doi.org/10.1016/j.jaci.2004.11.025
21. Lessard A, Alméras N, Turcotte H, Tremblay A, Després JP, Boulet LP. Adiposity and pulmonary function: Relationship with body fat distribution and systemic inflammation. Clin Investig Med. 2011;34(2):64-70. https://doi.org/10.25011/cim.v34i1.15102
22. Global initiative for asthma: Asthma management and prevention, 2019. Pract Nurse. 2019;49(5):9.
23. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes. 2012;7(4):284-94. https://doi.org/10.1111/j.2047-6310.2012.00064.x
24. Neyzi O, Bundak R, Gökçay G, et al. Reference values for weight, height, head circumference, and body mass index in Turkish children. JCRPE J Clin Res Pediatr Endocrinol. 2015;7(4):280-93. https://doi.org/10.4274/jcrpe.2183
25. Van Huisstede A, Castro Cabezas M, Van De Geijn GJM, et al. Underdiagnosis and overdiagnosis of asthma in the morbidly obese. Respir Med. 2013;107(9):1356-64. https://doi.org/10.1016/j.rmed.2013.05.007
26. King GG, Bates J, Berger KI, et al. Technical standards for respiratory oscillometry. Eur Respir J. 2020;55(2):1-21. https://doi.org/10.1183/13993003.00753-2019
27. Oostveen E, Boda K, Van Der Grinten CPM, et al. Respiratory impedance in healthy subjects: Baseline values and bronchodilator response. Eur Respir J. 2013;42(6):1513-23. https://doi.org/10.1183/09031936.00126212
28. Frei J, Jutla J, Kramer G, Hatzakis GE, Ducharme FM, Michael Davis G. Impulse oscillometry: Reference values in children 100 to 150 cm in height and 3 to 10 years of age. Chest. 2005;128(3):1266-73. https://doi.org/10.1378/chest.128.3.1266
29. Chinn S, Jarvis D, Burney P. Relation of bronchial responsiveness to body mass index in the ECRHS. Thorax. 2002;57(12):1028-33. https://doi.org/10.1136/thorax.57.12.1028
30. Bibi H, Shoseyov D, Feigenbaum D, et al. The relationship between asthma and obesity in children: Is it real or a case of over diagnosis? J Asthma. 2004;41(4):403-10. https://doi.org/10.1081/JAS-120026097
31. Yao TC, Tsai HJ, Chang SW, et al. Obesity disproportionately impacts lung volumes, airflow and exhaled nitric oxide in children. PLoS One. 2017;12(4):1-16. https://doi.org/10.1371/journal.pone.0174691
32. Forno E, Weiner DJ, Mullen J, et al. Obesity and airway dysanapsis in children with and without asthma. Am J Respir Crit Care Med. 2017;195(3):314-23. https://doi.org/10.1164/rccm.201605-1039OC
33. van de Kant KDG, Paredi P, Meah S, Kalsi HS, Barnes PJ, Usmani OS. The effect of body weight on distal airway function and airway inflammation. Obes Res Clin Pract. 2016;10(5):564-73. https://doi.org/10.1016/j.orcp.2015.10.005
34. Shore SA. Obesity and asthma: Possible mechanisms. J Allergy Clin Immunol. 2008;121(5):1087-93. https://doi.org/10.1016/j.jaci.2008.03.004
35. Maachi M, Piéroni L, Bruckert E, et al. Systemic low-grade inflammation is related to both circulating and adipose tissue TNFα, leptin and IL-6 levels in obese women. Int J Obes. 2004;28(8):993-7. https://doi.org/10.1038/sj.ijo.0802718
36. Vijayakanthi N, Greally JM, Rastogi D. Pediatric obesity-related asthma: The role of metabolic dysregulation. Pediatrics. 2016;137(5):e20150812. https://doi.org/10.1542/peds.2015-0812
37. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: A meta-analysis of prospective epidemiologic studies. Am J Respir Crit Care Med. 2007;175(7):661-6. https://doi.org/10.1164/rccm.200611-1717OC
38. Assumpção MS, Ribeiro JD, Wamosy RMG, Figueiredo FCXS, Parazzi PLF, Schivinski CIS. Impulse oscillometry and obesity in children. J Pediatr (Rio J). 2018;94(4):419-

24.
https://doi.org/10.1016/j.jped.2017.06.007
39. Kalhoff H, Breidenbach R, Smith HJ, Marek W. Impulse oscillometry in preschool children and association with body mass index. Respirology. 2011;16(1):174-9.
https://doi.org/10.1111/j.1440-1843.2010.01906.x
40. Ekström S, Hallberg J, Kull I, et al. Body mass index status and peripheral airway obstruction in school-age children: a population-based cohort study. Thorax. 2018;73(6):538-45.
https://doi.org/10.1136/thoraxjnl-2017-210716
41. Erkoçoğlu M, Kaya A, Özcan C, et al. The effect of obesity on the level of fractional exhaled nitric oxide in children with asthma. Int Arch Allergy Immunol. 2013;162(2):156-62.
https://doi.org/10.1159/000351454
42. Rastogi D, Canfield SM, Andrade A, et al. Obesity-associated asthma in children a distinct entity. Chest. 2012;141(4):895-905.
https://doi.org/10.1378/chest.11-0930
43. Sansone F, Attanasi M, Di Pillo S, Chiarelli F. Asthma and obesity in children. Biomedicines. 2020;8(7):1-16.
https://doi.org/10.3390/biomedicines8070231
44. Schachter LM, Peat JK, Salome CM. Asthma and atopy in overweight children. Thorax. 2003;58(12):1031-5.
https://doi.org/10.1136/thorax.58.12.1031
45. Tantisira KG, Litonjua AA, Weiss ST, Fuhlbrigge AL. Association of body mass with pulmonary function in the Childhood Asthma Management Program (CAMP). Thorax. 2003;58(12):1036-41.
https://doi.org/10.1136/thorax.58.12.1036
46. Hancox RJ, Milne BJ, Poulton R, et al. Sex differences in the relation between body mass index and asthma and atopy in a birth cohort. Am J Respir Crit Care Med. 2005;171(5):440-5.
https://doi.org/10.1164/rccm.200405-623OC