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The impact of adiposity indices on lung function in children with respiratory allergic diseases

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ABSTRACT

Introduction: The effect of obesity on lung function in children stratified by asthma status is not fully elucidated. We evaluated the impact of adiposity indices, including Body Mass Index (BMI) and estimated fat mass (eFT), on lung changes in asthmatic and non-asthmatic children with rhinitis.

Patients and Methods: We performed a retrospective review of 400 pediatric patients, classified into an asthma group (n = 200) and a no-asthma group (n = 200). According to the BMI z-score all subjects were classified into normal-weight patients (NW; $-2 \leq$ BMI z-score <1) and overweight patients/patients with obesity (OW/OB; BMI z-score ≥ 1). Lung function parameters were measured by spirometry. BMI and eFM were considered as adiposity indices.

Results: Excess weight/obesity was present in 37 % of patients. The OW/OB group showed higher basal forced expiratory vital capacity (FVC) and lower forced expiratory volume in 1 s (FEV_1), FEV_1/FVC ratio compared to the NW group ($p \leq 0.01$). FVC and FEV_1 were correlated with the BMI z-score, and FEV_1/FVC with eFT ($p \leq 0.01$). No differences were noted between the NW and the OW/OB groups in terms of respiratory parameters except for FVC ($p < 0.01$). In the OW/OB group, asthma patients were significantly different based on FEV_1, FEV_1/FVC, and forced expiratory flow at 25–75 % of FVC ($FEF_{25/75}$) ($p < 0.01$). The BMI z-score was correlated with FVC and FEV_1 in both the no-asthma and asthma groups ($p \leq 0.01$ and $p \leq 0.05$, respectively), while eFM was correlated with FEV_1/FVC ($p = 0.007$) in the asthma group only.

Conclusion: Obesity seems to have a significant impact on lung function in children with respiratory allergic diseases. BMI and eFM may be used to evaluate the impact of adiposity on lung function.

Introduction

Obesity is one of the most pressing public health problems worldwide [1,2]. As reported by the World Health Organization (WHO) in 2016, more than 340 million children and adolescents globally were living with excess body weight [1].

Obesity results from an excessive accumulation of body fat due to a positive energy balance and weight gain. It is also related to the interaction between genes, environment, lifestyle, and emotional factors [3]. It causes multiple complications such as severe organ and tissue derangements. The effects of obesity on the respiratory system include complex diseases such as asthma, obstructive sleep apnea, and chronic obstructive pulmonary disease [4,5].

Airway hyper-responsiveness, inflammation, and airway obstruction/remodeling are the main structural and anatomical features of asthma. Although it affects people of all ages, it disproportionately affects children [6]. Indeed, pediatric asthma is the most common allergic disease worldwide. According to the WHO, more than 262 million people had asthma in 2019 [7]. Asthma is associated with considerable morbidity, poorer quality of life for the patient and family, and economic burden. Lifestyle factors including obesity have been implicated as one of the many factors contributing to asthma [8].

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A high percentage of body fat in childhood represents an independent predictor of asthma. There is a relative risk of 1.2–1.8 for incident asthma in overweight/obesity [9,10].

However, whether obesity leads to asthma or vice versa is still debatable. Different mechanisms can be hypothesized to explain both directions in this relationship. Asthmatic children generally are less active than healthy children and receive treatments that increase their appetite and weight, putting them at risk of weight gain or obesity. In contrast, obesity is a process characterized by mild chronic inflammation and metabolic alterations which could affect lung mechanics, favouring asthma development [11,12].

Body mass index (BMI) is usually used as an index of adiposity; however, it does not discriminate between lean and fat mass. Recently, Hudda et al. reported [13] a model based on height, weight, age, sex, and ethnicity to predict fat mass in children. The estimated Fat mass (eFM) using the new formula has been associated with cardiovascular health [14] and metabolic profile [12] in overweight/obesity. Currently, there is no data correlating eFM with respiratory conditions.

Recent literature examining obesity and lung function in children without respiratory diseases remains conflicting [15]. Some studies evaluating the effect of obesity on lung function in children and adults, stratified by asthma status, showed differences between children and adults. However, all measures of lung function were decreased among subjects with obesity [6]. In the pediatric population, being overweight has a harmful effect on the forced expiratory volume in 1 s (FEV_1)/-forced expiratory vital capacity (FVC) ratio in children, regardless of asthma status. Additionally, there is a higher impact in healthy, non-asthmatic children [6]. Very few studies have assessed the effects of being overweight/obesity on lung function in children with allergic rhinitis (AR) [16].

The aim of this study was to evaluate the impact of adiposity indices, including BMI and eFT, on lung function in children with respiratory allergic diseases (e.g., persistent allergic rhinitis) without asthma, compared to asthmatic patients.

Patients and methods

Patients

We performed a retrospective review of medical records of 400 children and adolescents. They were classified into two groups (200 in the asthma group and 200 in the no-asthma group). They were referred to the Allergy Unit at Buzzi Children's Hospital between January 2016 and December 2019 for clinical evaluation.

In all patients, auxological evaluation and lung function parameters were recorded. BMI and eFM were considered as adiposity indices.

According to the Global Initiative for Asthma (GINA) report, asthma is diagnosed based on the clinical history of respiratory symptoms (wheezing, shortness of breath, chest tightness, coughing) associated with a variable expiratory airflow limitation, confirmed by spirometry before and after bronchodilator administration (reversibility testing) [17]. In contrast, AR is diagnosed based on medical history and clinical examination with normal lung function on spirometry.

In both groups atopy was detected by the skin prick test. Most of our patients were sensitized to aeroallergens.

Personalized therapy was prescribed for asthmatic patients according to the GINA Guidelines [17] and for non-asthmatic subjects with rhinitis according to the Allergic Rhinitis and its Impact on Asthma Guidelines [18].

Patients with cardiovascular diseases and respiratory chronic diseases other than asthma were excluded from the analysis.

For statistical analysis, the patients were classified into four groups according to the BMI z-score WHO classification and the presence of asthma: normal-weight patients (NW) without asthma;.

overweight patients/patients with obesity (OW/OB) without asthma; NW with asthma; OW/OB with asthma.

Data were retrospectively evaluated according to the principles of the Declaration of Helsinki as revised in 2008. Ethical committee approval was not requested because the General Authorization to Process Personal Data for Scientific Research Purposes (Authorization no. 9/2014) declared that ethics approval is not needed for retrospective archive studies that use ID codes, preventing the data from being traced back directly to the data subject. The privacy of the collected information was ensured according to Regulation (EU)/2016/679 GDPR (Regulation (EU) 2016/679), Legislative Decree n.101/18. Informed consent was not obtained, as this was a retrospective study; however, the anonymity of the patients was preserved.

Methods

In all patients, weight, standing height, and the stage of puberty according to Marshall and Tanner were measured [19,20].

Weight and standing height were recorded as previously reported [21]. Pubertal stages were classified as follows, prepubertal stage = Tanner Stage 1; middle puberty = Tanner Stages 2–3; late puberty = Tanner Stages 4–5.

BMI was calculated as body weight (kilograms) divided by the square of the height (meters squared) and was transformed into BMI z-scores using WHO reference values [22]. According to the BMI z-score WHO classification [22], all subjects were classified into NW ($-2 \leq$ BMI z-score <1) and OW/OB (BMI z-score ≥ 1/BMI z-score ≥ 2, respectively).

The eFM was calculated using the following formula: Fat Mass = eight $-$ exp[0.3073 $\times$ height^2 $-$ 10.0155 $\times$ weight$-$ 1 + 0.004571 $\times$ weight + 0.01408 $\times$BA $-$ 0.06509 $\times$SA $-$ 0.02624 $\times$AO $-$ 0.01745 $\times$ other$-$ 0.9180 $\times$ ln(age) + 0.6488 $\times$age$^{0.5}$ + 0.04723 $\times$male + 2.8055] (exp = exponential function, ln = natural logarithmic transformation, score 1 if a child was of black (BA), south Asian (SA), other Asian (AO), or other (other) ethnic origin and score 0 if not. If a child was of an unknown ethnic group, it was treated as of white ethnic origin. Height was measured in meters, weight in kilograms, age in years, and fat mass in kilograms) [14].

Lung function

Lung function parameters, including FVC, FEV_1, FEV_1/FVC, and forced expiratory flow at 25–75% of FVC ($FEF_{25/75}$) were measured by spirometry (COSMED MicroQuark spirometer).

Statistical analysis

Data were summarized as frequencies and percentages if categorical, and as means and standard deviation (SD) or median and IQR (interquartile range) if continuous. The Shapiro–Wilk test was used to test the normality of data. Fisher's exact test was used to assess the association between categorical variables. T-test was used to assess the differences in respiratory parameters between the weight (NW vs OW) and asthma (yes vs no) groups. A correlational analysis was performed (Pearson or Spearman according to the achieved normality) to determine the possible relationship between markers of body fat and respiratory parameters. A p-value < 0.05 was considered significant. All statistical analyses were performed using Stata software v 16.1 (StataCorp USA).

Results

Clinical features

The clinical features of the enrolled patients (258 males and 142 females; mean age 9.55 $\pm$ 0.13 yrs) are reported in Table 1. The asthma and no-asthma groups were similar in age, sex, and pubertal stages. No significant differences was noted in the adiposity indices (BMI z-score and fat mass) between the two groups [($p > 0.05$), Table 1].

Excess weight/obesity was present in 148/400 (37 %) of the patients,

Table 1
Clinical and respiratory parameters in patients with and without asthma.

	All	Asthma	No-asthma	p*
Age (years)	9.55 ± 2.72	9.41 ± 2.65	9.69 ± 2.78	0.31
Sex (M/F)	258/142	132/68	126/74	0.53
BMI z-score	0.58 ± 1.27	0.64 ± 1.31	0.53 ± 1.23	0.38
Fat mass	9.93 ± 5.57	10.0 ± 5.27	9.82 ± 5.43	0.68
Pubertal stages (n)				
	195	103	92	0.53
• prepubertal stage	164	77	87	
• middle puberty	41	20	21	
• late puberty				

The association of categorical variables was assessed using the Fisher's exact test. The T- test was used to assess the differences in continuous parameters between asthma and no-asthma groups.
* asthma vs non-asthma

without any difference in age, sex, and pubertal stages compared to NW subjects ($p > 0.05$), as shown in Table 2.

Lung function parameters

As reported in Table 2, the OW/OB group showed higher basal FVC ($p < 0.01$) and FEV_1 ($p = 0.07$) and lower FEV_1/FVC ($p < 0.004$) compared with the NW group. FVC ($r = 0.16$, $p < 0.001$) and FEV_1 ($r = 0.12$, $p = 0.01$) were significantly correlated with the BMI z-score. FEV_1/FVC ($r = -0.13$, $p < 0.001$) was significantly correlated with eFT.

Based on the presence of asthma, no significant differences were noted in the respiratory parameters between the NW and OW/OB groups, except for FVC ($p < 0.01$), as shown in Table 2. No sex differences in spirometric indices were observed according to BMI groups.

In the OW/OB group, significant differences in FEV_1, FEV_1/FVC, and $FEF_{25/75}$ were observed between asthmatic and non-asthmatic patients ($p < 0.01$, Table 2). There were no differences noted in the FVC ($p = 0.26$).

In the NW group, all lung function parameters were significantly different between asthmatic and non-asthmatic patients ($p < 0.01$). Lung function parameters and adiposity indices were significantly correlated in both groups, as shown in Table 3. BMI z-score was significantly correlated with both FVC ($r = 0.18$, $p = 0.007$ and $r = 0.16$, $p = 0.01$, respectively) and FEV_1 ($r = 0.18$, $p = 0.01$ and $r = 0.13$, $p = 0.05$, respectively) in the no-asthma and asthma group. In the asthma group, eFM was significantly correlated with FEV_1/FVC ($r = -0.21$, $p = 0.007$).

Discussion

Obesity is recognized as a risk factor for asthma, with a relative risk estimated at 1.29 (95 % CI: 1.16–1.42), and reports showing that obesity induces 23–27 % of asthma cases in children [23].

A significant difference was noted in respiratory parameters between the OB/OW group compared to the NW subjects and in asthma vs no-asthma subjects. A correlation between these parameters and adiposity indices, such as BMI and eFM, was noted. These imply that obesity has an important role on lung function.

Consistent with previous literature [24–27], we noticed that FVC was higher in OW/OB children compared to NW children. OW/OB children also exhibited relatively higher FEV_1 values (without reaching statistical significance) and significantly lower FEV1/FVC ratio compared to NW children. However, another study contradicted our results [28].

Our findings support the hypothesis that being overweight is associated with airflow obstruction due to increased airway resistance [25–27].

In adults, patients with obesity have a lower functional residual capacity and tidal volume, mainly due to the changes in the elastic structural properties of the chest wall [29]. In children, the most relevant effect of adiposity is the decline in the FEV_1/FVC ratio with a higher FVC [30].

This effect can be explained by the so-called "dysanapsis". During childhood, obesity influences the lung volume differently as a consequence of disproportion between the growth of the parenchyma and the caliber of the airway. Indeed, the FEV_1/FVC ratio is reduced, although the values of both FVC and FEV_1 are within normal limits [23,31–33].

Moreover, $FEF_{25/75}$ value was not significantly different between OW/OB and NW. This finding is not surprising as this parameter does not play a significant role in measuring airflow obstruction, as assessed by the American Thoracic Society parameters [34]. In fact, the $FEF_{25/75}$ value is of limited diagnostic value in detecting airway obstruction in clinical practice due to its variability [35].

The effects of body fat on lung function in children have recently been reported [24]. Bioelectrical impedance, magnetic resonance imaging, and dual energy X-ray absorptiometry can be employed to assess body composition. However, these tools are expensive and difficult to use in routine clinical practice. Even though BMI is not a direct measure of body fat, it is conventionally accepted as an index of adiposity [36].

Recently, a new non-linear equation which estimates fat mass, taking into account weight, height, ethnic origins, and age has been proposed [13].

In our study, a significant correlation between adiposity indices and

Table 2
Clinical characteristics and lung function parameters (pre-bronchodilatation) in asthma and no-asthma groups, according to weight.

	Groups								
	All			Asthma			No-asthma		
	NW	OW/OB	p	NW	OW/OB	p	NW	OW/OB	p
Age	9.61 ± 2.89	9.44 ± 2.39	0.54	9.57 ± 2.81	9.14 ± 2.35	0.26	9.65 ± 2.98	9.75 ± 2.41	0.80
Sex (M/F)	156/96	102/46	0.15	73/52	53/22	0.08	83/44	49/24	0.79
BMI z-score	-0.18 ± 0.81	1.89 ± 0.74	< 0.001	-0.16 ± 0.81	1.89 ± 0.78	< 0.001	-0.20 ± 0.81	1.80 ± 0.69	< 0.001
Fat mass	7.21 ± 2.9	14.57 ± 5.97	< 0.001	7.32 ± 2.98	14.58 ± 6.31	< 0.001	7.09 ± 2.81	14.56 ± 5.64	< 0.001
Pubertal stages									
	127	68	0.06	64	39	0.07	63	29	0.29
• prepubertal stage	4	70		44	33		50	27	
• middle puberty	31	10		17	3		14	7	
• late puberty									
FVC (%)	91.55 ± 10.34	94.95 ± 11.49	p < 0.01	89.25 ± 10.73	93.90 ± 11.67	< 0.01	93.81 ± 9.46 *	96.04 ± 11.28	0.13
FEV_1 (%)	89.26 ± 10.97	91.42 ± 12.67	p = 0.07	83.72 ± 10.01	86.58 ± 12.50	0.07	94.71 ± 8.99 *	96.39 ± 10.86 *	0.24
FEV_1/FVC (%)	85.44 ± 8.55	83.56 ± 9.98	p = 0.04	82.00 ± 9.73	79.51 ± 11.44	0.10	88.82 ± 5.39 *	87.72 ± 5.84 *	0.18
$FEF_{25/75}$ (%)	79.08 ± 7.33	79.28 ± 8.40	p = 0.80	67.64 ± 15.84	68.57 ± 18.28	0.70	90.34 ± 17.17 *	90.97 ± 21.22 *	0.82

NW= normalweight; OW/OB= overweight/obese
*Statistically significant difference ($p < 0.01$) in NW and OW/OB groups comparing asthma vs no-asthma groups. The T- test was used to assess the differences in respiratory parameters between the groups (NW vs OW) and asthma (yes vs no).

Table 3
Correlation between body mass index (BMI) z score and estimated fat mass (eFT) according to the presence of asthma.

	No-asthma				Asthma			
	BMI-z score		eFM		BMI-z score		eFM	
	r	p	r	p	r	p	r	p
Basal FVC (%)	0.18	< 0.01	0.08	0.20	0.16	0.01	0.01	0.86
Basal FEV_1 (%)	0.18	0.01	0.03	0.59	0.18	0.13	-0.06	0.38
Basal FEV_1/FVC (%)	-0.03	0.57	-0.10	0.15	-0.12	0.06	-0.21	< 0.01
Basal $FEF_{25/75}$ (%)	0.09	0.17	0.003	0.95	0.02	0.76	-0.10	0.15

lung function parameters was found. BMI is correlated to FVC but not to FEV_1/FVC, while eFM is significantly associated with FEV_1/FVC in the asthma group. These suggest that adiposity indices may be useful in clinical practice.

Further confirmation by subsequent studies should make this tool more suitable than body impedance analysis (BIA). This is not always available and/or difficult to use, requiring technical expertize and dedicated personnel.

The authors acknowledge that the study has some limitations. First, it is a retrospective study and the results may be affected by some bias. Second, there was no data on adiposity distribution. A comparison between the eFM and fat mass estimated through bioimpedance could improve the validity of the model. Finally, metabolic profiles and dietary behavior were not recorded. These aspects could influence respiratory function.

The strengths of the study include evaluation of patients with respiratory allergic diseases, inclusion of non-asthmatic children with rhinitis; inclusion of other adiposity indices aside from BMI; and inclusion of pubertal status as a possible confounding variable.

In conclusion, being overweight/obesity negatively affects lung function both in asthmatic and non-asthmatic children with allergic rhinitis. Both mechanical and immunomodulatory factors may play a role in the pathogenic mechanism. Aside from BMI, eFM is a viable indicator of adiposity in clinical practice. If these findings are confirmed by further studies, adiposity measures should be considered when managing respiratory allergic diseases in children.

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Ethical Statement

The data for this Research Paper were collected in accordance with the Declaration of Helsinki.

Author Agreement Statement

We the undersigned declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We understand that the Corresponding Author is the sole contact for the Editorial process. She is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

Conflicts of Interest

The authors declare no conflict of interest.

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