

# Obesity and Asthma: association or epiphenomenon?

*Obesidade e asma: associação ou epifenômeno?*

*Obesidad y asma: ¿asociación o epifenómeno?*

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## ABSTRACT

**Objective:** To relate obesity and asthma by comparing gender, age, initial classification of asthma, clinical control, basal forced expiratory volume in one second (FEV1) and forced expiratory flow between 25 and 75% (FEF25-75%) with rates of body mass index (BMI) in asthmatic adolescents.

**Methods:** Cross-sectional study involving 120 asthmatics patients (1.9 male: 1 female) with a mean age of 14.1 years (9 to 20.1 years of age), classified according to asthma severity and control, and evaluated by spirometry using their basal FEV1 and FEF25-75%. The data were described by frequency, mean and standard deviation or median and range and analyzed by ANOVA, unpaired *t* test, Fischer's exact test, Kruskal-Wallis and Pearson's correlation, considering significant  $p < 0.05$ .

**Results:** There was no difference between gender in relation to the initial classification and the level of asthma control; 91.7% (100 cases) received initial classification as persistent and 106 cases (88.3%) were partially or totally controlled. There was no statistical difference between controlled patients and the others in relation to BMI. No significant correlations were found between zBMI and FEV1 and between zBMI and FEF25-75%, analyzing all patients and only patients with overweight or obese.

**Conclusions:** In this study, no significant correlation was found between overweight/obesity and asthma using clinical, anthropometric and spirometric parameters.

**Key-words:** adolescent; obesity; overweight; asthma; spirometry.

## RESUMO

**Objetivo:** Avaliar a associação entre obesidade e asma pela comparação entre idade, gênero, classificação inicial e controle da asma, valores de volume expiratório forçado no primeiro segundo (VEF1) e fluxo expiratório forçado entre 25 e 75% (FEF25-75%) basais com os índices de massa corpórea (IMC) em adolescentes asmáticos.

**Métodos:** Estudo transversal envolvendo 120 pacientes (1,9 masculino:1 feminino) asmáticos com mediana de idade de 14,1 anos (9 a 20,1 anos), classificados quanto ao controle e gravidade da asma e avaliados pela espirometria utilizando VEF1 e FEF25-75% basais. Esses dados foram descritos pela frequência, médias e desvio padrão ou medianas e variação, sendo analisados pelos testes de ANOVA, teste *t* não pareado, teste exato de Fisher, Kruskal-Wallis e pela correlação de Pearson, considerando-se significativa  $p < 0,05$ .

**Resultados:** Não houve diferença entre os gêneros em relação à classificação inicial da asma e ao nível de controle. Receberam classificação inicial persistente 91,7% (100 casos), sendo que 106 casos (88,3%) encontravam-se parcial ou totalmente controlados. Não houve diferença estatística entre os pacientes controlados e os demais em relação ao IMC. Não foram encontradas correlações significantes entre zIMC e VEF1 e entre zIMC e FEF25-75%, analisando-se todos os pacientes e apenas pacientes com sobrepeso ou obesos.

**Conclusões:** Neste estudo, não foi encontrada correlação significativa entre sobrepeso/obesidade e asma,

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utilizando-se parâmetros clínicos, antropométricos e espirométricos.

**Palavras-chave:** adolescente; obesidade; sobrepeso; asma; espirometria.

## RESUMEN

**Objetivo:** Evaluar la asociación entre obesidad y asma por la comparación entre edad, género, clasificación inicial y control del asma, valores de volumen espiratorio forzado en el primer segundo (VEF1) y flujo espiratorio forzado entre 25 y 75% basal (FEF25-75%) con los índices de masa corporal (IMC) en adolescentes asmáticos.

**Métodos:** Estudio transversal implicando a 120 pacientes (1,9M:1F) asmáticos con mediana de edad de edad de 14,1 años (9 a 20,1 años), clasificados respecto al control y gravedad del asma, y evaluados por la espirometría utilizando su VEF1 y FEF25-75% basales. Estos datos fueron descriptos por la frecuencia, promedios y desviaciones estándar o medianas y variación y analizados por las pruebas de ANOVA, prueba t no pareada, Prueba exacto de Fisher, Kruskal-Wallis y por la correlación de Pearson considerándose significantes valores de  $p < 0,05$ .

**Resultados:** No hubo diferencia entre los géneros respecto a la clasificación inicial del asma y el nivel de control. Recibieron clasificación inicial persistente 91,7% (100 casos), siendo que 106 casos (88,3%) estaban parcial o totalmente controlados. No hubo diferencia estadística entre los pacientes controlados y los restantes respecto al IMC. No se encontraron correlaciones significantes entre zIMC y VEF y entre zIMC y FEF25-75% al analizar todos los pacientes y solamente los pacientes con sobrepeso u obesos.

**Conclusiones:** En este estudio, no fue encontrada correlación significativa entre sobrepeso/obesidad y asma, utilizándose parámetros clínicos, antropométricos y espirométricos.

**Palabras clave:** adolescente; obesidad; sobrepeso; asma; espirometría.

## Introduction

In recent years, there has been a progressive increase in the prevalence of obesity in children in Brazil<sup>(1-3)</sup>. According to data from the Surveillance System of Protective and Risk Factors for Chronic Diseases by Telephone Survey (VIGITEL 2011)<sup>(1)</sup>, the frequency of obesity in adults increased from 11.4% in 2006, to 15.8% in 2011. The percentage of 48.5% overweight Brazilians

are also noteworthy. Regarding the pediatric age range, the number of overweight children in the country increased between 2008 and 2009, according to the Household Budget Survey conducted by the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística – IBGE). In this short period, the number of obese children from 5 to 9 years old increased more than 300%. In the age group from 10 to 19 years, the frequency of overweight ranged, on average, from 10.8% in 2008 to 20% in 2009<sup>(2)</sup>.

Asthma is also a prevalent disease in our country<sup>(4)</sup> and its association with obesity is subject of many studies, but the nature of this association remains unclear<sup>(5-7)</sup>. The project International Study of Asthma and Allergies in Childhood (ISAAC), in its phase III, was performed in several Brazilian cities between the years 2001 and 2005 and showed a prevalence of asthma in adolescents from 13 to 14 years in Brazil between 21–22%, data that resemble the prevalence in other countries, where asthma also has a significant impact on public health<sup>(4)</sup>.

Some cross-sectional or prospective studies conducted in children and adults sustained a relationship between obesity and asthma<sup>(8)</sup>. Epidemiological studies associate obesity with increased incidence and prevalence of asthma, being asthma usually preceded by obesity<sup>(9,10)</sup>. However, the association between asthma and obesity remains controversial, and the results of the studies are conflicting<sup>(9,11-13)</sup>.

The aim of this study was to assess the association between body mass index (BMI) and age, gender, initial classification of asthma severity, disease control, forced expiratory volume in 1 second (FEV1) and baseline forced expiratory flow between 25 and 75% (FEF25-75%) in asthmatic adolescents receiving usual treatment for asthma.

## Method

This is a cross-sectional study, including 120 asthmatic patients from 9 to 20.1 years who were followed up at in the asthma and rhinitis outpatient clinic at the Allergy and Immunology Unit of Children's Institute at HCFMUSP (Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo). The participants were submitted to complete clinical evaluation, including general and specific physical examinations, with special attention to the upper and lower airways. The skin, eyes, cardiovascular system, and abdomen were examined, followed by weight, height, blood pressure (BP), and peak expiratory flow (PEF) measurements. Adherence to treatment and inhalation techniques were also checked. The patients were

classified according to asthma severity and control. A pulmonary function test (PFT) was also carried out.

These patients were initially classified according to asthma severity into four groups: intermittent asthma (IA), mild persistent asthma (MiPA), moderate persistent asthma (MoPA), or severe persistent asthma (SPA). They were also evaluated according to the level of asthma control and divided into controlled (C), partly controlled (PC) or uncontrolled (U) as defined in Global Initiative for Asthma (GINA)<sup>(14)</sup>.

Weight was measured using a platform scale with digital display, a capacity range from 2 to 180kg and a resolution of 100g (Filizola<sup>®</sup>, model Personal PL 180, São Paulo, SP, Brazil). The child was weighed barefoot and in minimal clothing, standing straight in the center of the equipment, feet together and arms extended alongside the body, remaining in this position until measurements were completed<sup>(15)</sup>. For height evaluation, a stadiometer with capacity of 0.4–2.2m and a resolution in millimeters was used (Sanny<sup>®</sup>, São Paulo, SP, Brazil). The child stood straight on the center of the equipment, barefoot, without with hair accessories, arms alongside the body, head up, staring at a fixed point at eye level. The examiner made sure the heels, buttocks, and shoulders were in contact with the anthropometer, and that the inner sides of the heels and knees were touching. The feet were kept at a right angle with the leg<sup>(15)</sup>. Body mass index (BMI=ratio of weight and height squared) was calculated, and classified by Z-score according to the World Health Organization (WHO)<sup>(16)</sup> standard curve of 2007. Calculations were made using the AnthroPlus software, developed by the WHO<sup>(17)</sup> in 2009. The Z-scores were used to classify obesity into three groups, according to the

gender-specific National Center for Health Statistics<sup>(18)</sup> curves: 85<sup>th</sup>–94.9<sup>th</sup> percentile – overweight; ≥95<sup>th</sup> percentile – obesity; <85<sup>th</sup> percentile – all patients who did not fall into these two other categories.

We calculated the Z-score indexes using the WHO<sup>(17)</sup> software. Patients with endocrine problems or other syndromes associated with obesity or overweight were excluded.

Spirometry was performed using a Survey spirometer (W.E. Collins, Braintree, state of MA, USA). The measurements selected for analysis were the forced expiratory volume in one second (FEV1) and the forced expiratory flow between 25 and 75% of forced vital capacity (FEF 25–75%) at baseline<sup>(19,20)</sup>.

Data were expressed as frequency or mean and standard deviation each time the distribution was normal by the Kolmogorov-Smirnov test. The variables that did not show normal distribution in at least one of the analyzed parameters (age, BMI, BMI<sub>p</sub>, BMI<sub>z</sub>, FEV1, FEF25–75%), were expressed as median (minimum-maximum). To compare the mean age among groups distributed by BMI<sub>p</sub> the ANOVA test was used. Fisher's exact test was used for the analysis of nominal variables such as gender, initial classification and asthma control in both BMI<sub>p</sub> groups (BMI<sub>p</sub><85% and BMI<sub>p</sub>≥85%). The Kruskal-Wallis test (non-parametric ANOVA) was used to compare baseline, BMI<sub>p</sub>, BMI<sub>z</sub>, FEV1 and FEF25–75 medians in relation to BMI<sub>p</sub> values. The correlations (Pearson) between BMI<sub>z</sub> and FEV1 and BMI<sub>z</sub> and FEF25–75% were assessed. All analyses were performed using the Statistical Package for the Social Sciences – SPSS version 13.0. Significance values were set at  $p < 0.05$ .

All patients received medication for asthma crisis control and maintenance (recommended by consensus agreements)

**Table 1** - Demographic data, initial classification and asthma control according to BMI<sub>p</sub> in 120 patients

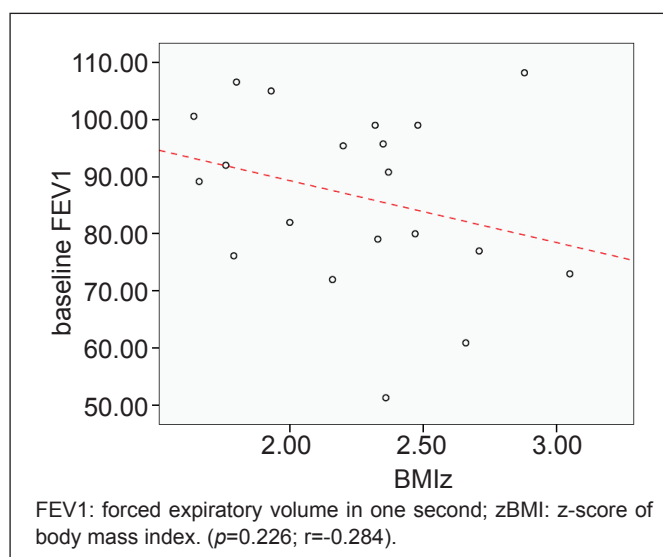
Variable	Total n=120	BMI <sub>p</sub> <85% n=82	BMI <sub>p</sub> ≥85% n=38	p
Age (years)	14.1 (9.7–20.1)	13.9 (9.7–19.3)	14.1 (9.9–20.1)	0.874*
Gender				
M	78 (65.0)	57 (69.5)	21 (55.3)	0.152 <sup>‡</sup>
F	42 (35.0)	25 (30.5)	17 (44.7)	
Initial classification of asthma				0.448 <sup>‡</sup>
I + MiPA	22 (18.3)	17 (20.7)	5 (13.2)	
MoPA + SPA	98 (81.7)	65 (79.3)	33 (86.8)	
Asthma control				0.152 <sup>‡</sup>
C	78 (65.0)	57 (69.5)	21 (18.0)	
PC/ UC	42 (35.0)	25 (30.5)	17 (14.0)	

Data expressed as median (minimum-maximum) and n (%); \*ANOVA; <sup>‡</sup>Fisher's exact test. BMI<sub>p</sub>: body mass index percentile; M: male; F: female; I: intermittent; MiPA: mild persistent asthma; MoPA: moderate persistent asthma; SPA: severe persistent asthma; C: controlled; PC: partly controlled; UC: uncontrolled

**Table 2** - Distribution of values of BMI, BMIp and BMIz, baseline FEV1 and FEF 25–75% according to BMI in 120 patients with asthma

Variable	Total (n=120)	BMIp<85% (n=82)	BMIp≥85% (n=38)	p*
BMI	19.7 (14.2–35.0)	18.1 (14.2–23.6)	25.6 (19.4–35.0)	<0.0001
BMIp	62.9 (0.0–100.0)	45.4 (0.0–83.9)	94.6 (85.5–100.0)	<0.0001
BMIz	0.28 (-3.71–3.10)	-0.12 (-3.71–0.99)	1.8 (1.10–3.10)	<0.0001
FEV1	82.2 (46.6–153.6)	82.2 (46.6–153.6)	85.9 (51.3–127.0)	0.664
FEF25-75%	64.9 (19.1–169.4)	65.9 (19.1–169.4)	65.1 (23.9–116.0)	0.972

Data expressed as median (minimum- maximum); \*Kruskal-Wallis test. BMI: body mass index; FEV1: forced expiratory volume in 1 second; FEF25–75%: baseline forced expiratory flow between 25 and 75%



**Figure 1** - Correlation between BMI Z-score (BMIz) and baseline values of FEV1 (expressed as percentages of predicted values for gender and height) in obese asthmatic patients

free of cost. They returned every two months or whenever necessary and were questioned each time about symptoms, medication used, visits to the emergency department, drug application techniques and adherence to treatment.

This study was approved by the Research Ethics Committee of HCFMUSP (CAPPesq) under protocol number 0367/2008.

## Results

There was a predominance of male participants (65%). Age had a similar mean between the genders ( $14.5 \pm 2.3$  for male and  $14.5 \pm 2.6$  for female participants; unpaired t test:

$p=0.942$ ). The distribution of the populations was normal. There was no statistical difference between the mean age of patients with BMIp<85% and those overweight and obese (BMIp≥85%) (ANOVA;  $p=0.874$ ) (Table 1).

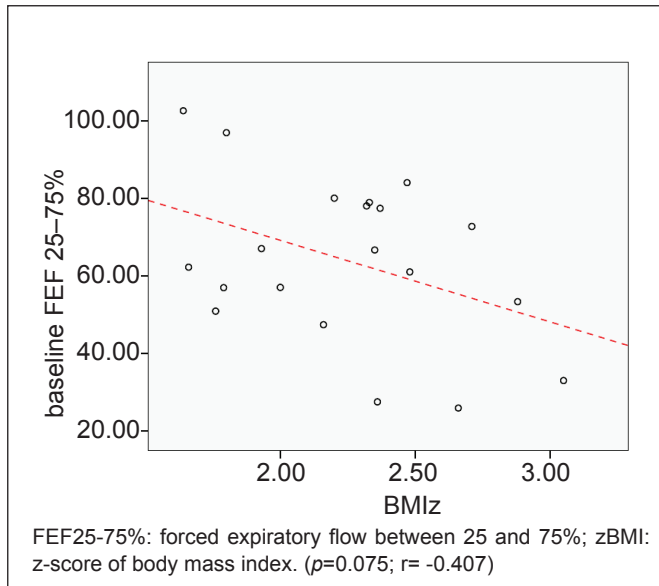
Among the analyzed patients, overweight was found in 15% (n=18) and obesity in 16.7% (n=20). There was no significant difference between genders regarding the BMIp values ( $p=0.152$ ) (Table 1).

Regarding the initial classification of asthma, most patients had persistent asthma, with 81.7% of cases being either moderate or severe (78 moderate persistent and 20 severe persistent). As for the initial classification of patients, there was no difference in relation to BMIp between intermittent + mild persistent and moderate persistent + severe persistent patients ( $p=0.448$ ). (Table 1).

At the moment of data collection, asthma was controlled (78 cases – 65%) or partly controlled (28 cases – 23.3%) in most cases. The reduced number of uncontrolled patients in each BMIp subgroup (eight cases with BMIp <85%; one case with BMIp between 85 and 94.9% and 5 cases with BMIp≥95%) hindered an adequate statistical analysis by the chi-square test. When comparing the different BMIp groups among the controlled patients and among all others (partly controlled and uncontrolled), no statistical difference was found ( $p=0.152$ ) (Table 1).

There was no difference between genders in relation to the initial classification of asthma (chi-square;  $p=0.777$ ) and to the level of asthma control (chi-square;  $p=0.387$ ).

Table 2 shows medians, minimum and maximum values of BMI, BMI percentile (BMIp) and Z-score of BMI (BMIz). It also shows medians, minimum and maximum



**Figure 2** – Correlation between BMI z-score (BMIz) and baseline values of FEF25–75% (expressed as percentages of predicted values for gender and height) in obese asthmatic patients

values of baseline FEV1 and FEF25–75%. There was a significant difference in BMI, BMI<sub>p</sub> and BMI<sub>z</sub> medians among the different BMI<sub>p</sub> groups ( $p < 0.0001$ ). There was no significant difference between the FEV1 and FEF25–75% values regarding their distribution among the BMI<sub>p</sub> groups ( $p > 0.05$ ) (Table 2).

There was no significant Pearson correlation between BMI<sub>z</sub> and FEV1 ( $r = 0.113$ ;  $p = 0.236$ ) and between BMI<sub>z</sub> and FEF25–75% ( $r = 0.001$ ;  $p = 0.988$ ), considering the overall group of patients. When only obese patients were analyzed (BMI<sub>p</sub> ≥ 95%), the correlation between BMI<sub>z</sub> and FEV1 became negative, but without statistical significance ( $r = -0.284$ ;  $p = 0.226$ ). The same occurred with the correlation between BMI<sub>z</sub> and FEF25–75% ( $r = -0.407$ ;  $p = 0.075$ ) (Figures 1 and 2).

## Discussion

The relationship between obesity and asthma is associated with physiological changes secondary to the presence of overweight<sup>(21)</sup>. In obese adults, the values of FEV1 and forced vital capacity are often limited. In children and adolescents, however, this pattern is not observed, with similar values found in obese and non-obese patients<sup>(22-25)</sup>. Peters *et al*, analyzing 473 children with asthma (66% with persistent

moderate and severe asthma and 28% obese) found that obesity was not associated with asthma severity, lung function, quality of life, or health care utilization<sup>(24)</sup>.

In this study no significant correlation was found between values of BMI/BMI<sub>z</sub> and FEV1 and FEF 25–75% in children and adolescents with asthma. When only obese patients were analyzed (BMI<sub>p</sub> ≥ 95%), the correlation between BMI<sub>z</sub> and FEV1/FEF25–75% became negative, but not statistically significant. In a study by Rodrigues *et al*, analyzing only 20 obese or overweight children, there was a better correlation between percentage reduction of FEF25–75% with the values of BMI, after bronchial provocation test with exercise, but this correlation was not significant either<sup>(26)</sup>.

Similar results were presented in a study by Lopes *et al*, in 2009, in which similar baseline values of FEV1 were found<sup>(27)</sup> in obese and non-obese asthmatic patients. A study conducted by Clerisme-Beaty *et al*<sup>(28)</sup> found no association between BMI and asthma control, although the authors used questionnaires that assessed only clinical parameters.

In Brazil, a cross-sectional study conducted in 2003 by Cassol *et al* with 4,010 adolescents from 13 to 14 years found positive association between obesity and the increase in the prevalence and severity of asthma symptoms<sup>(29)</sup>. In this study, the confirmation of asthma was based on the positive responses in the questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC), without medical confirmation. In contrast, our study showed no association between obesity and severity of asthma, even with 81.7% patients presenting moderate or severe asthma. This fact can be explained by the small sample of obese and overweight patients in this study. Brandão *et al*, in two studies conducted in asthmatic participants of a control program in the city of Feira de Santana, state of Bahia, also found no association of asthma severity with overweight and obesity, and there were no higher risks of hospitalization or exacerbations with visit to the emergency room in this group of asthmatics<sup>(30,31)</sup>.

Chin *et al*<sup>(32)</sup> found that obesity increases the risk of subsequent asthma, which has a higher incidence in women. In the present study, there was a predominance of male patients, and age had a similar mean between the genders. There was no difference between genders regarding the initial classification of asthma and between the level of asthma control.

The correlation between asthma and obesity may be determined by genetic and environmental factors. In obese patients, the decreased functional residual capacity and



expiratory reserve volume, as well as hormonal changes and cytokines may aggravate asthma according to the study conducted by Shore in 2007<sup>(33)</sup>. In a recent review Farah and Salome showed the possible mechanisms of the association between asthma and obesity, and that could be due to comorbidities associated with obesity, gastroesophageal reflux disease and obstructive sleep apnea and not properly obesity<sup>(34)</sup>.

Brenner *et al*<sup>(35)</sup> compared a group of 265 asthmatics with 482 healthy children in the same age group in relation to the prevalence of obesity in asthmatics and asthma severity. The authors concluded that there was no significant association between obesity and moderate/ severe asthma in Afro-American adolescents. In an Italian study, performed by Vignolo *et al*<sup>(36)</sup> with 554 children asthmatic and 652 healthy children, there was no increase in the prevalence of overweight/obesity in children and adolescents with asthma.

The present study has limitations related to the number of obese/overweight patients, which hinders the analysis of the relationship between asthma and obesity. Because it is a cross-sectional study, a great amount of data that

could have influenced the results were not analyzed. One of these aspects is pubertal staging, which could influence lung function tests. Other aspects such as race, color, smoking, early menarche, and concomitant diseases could not be analyzed due to the study design, which limits the multifactorial analysis that asthma and obesity may present. Prospective studies with a large number of patients may demonstrate the potential effect of overweight and obesity in the development of asthma and their relationship with severity and difficulty of control. If we take into account the percentage of overweight and obesity in populations that reach values close to 50%, as has happened in Brazil, the chance of developing asthma among these patients can be considered an accidental effect of the increased epidemic prevalence of obesity in populations.

In summary, as it can be observed in this and other analyzed studies, the relationship between asthma and obesity remains controversial, and it is still not clear whether there is an association between the increased rates of obesity and asthma, or whether they depend on external environmental factors or other endocrine variables.

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