Obesity and asthma: association or coincidence?
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Abstract

Objective: Asthma and obesity are among the major causes of morbidity in childhood and adolescence. Early obesity increases the chances of chronic degenerative diseases in adults. Although the concomitance or both clinical situations are being demonstrated in various studies, the intrinsic mechanisms of this association are still very little known. Therefore, the objective of this article was to review the main studies on the association of obesity and asthma and check if there is a cause-effect relation between them.

Sources: Systematic review based on indexed data bases MEDLINE (PubMed) and SciELO. Original articles (cross-sectional, case-control, and prospective studies) and meta-analysis published in the period that ranges from January 1998 to January 2008 were reviewed. Studies published in English, Spanish, and Portuguese were researched.

Summary of the findings: Although there are various studies on growing prevalence of asthma and obesity, few of them establish cause-effect relations between them. Physiopathological mechanisms and factors involved in this process are still little known.

Conclusion: Methodological rigor in future studies must seek for answers to better understand if there is association between asthma and obesity or if the relationship between both diseases is a coincidence.


Introduction

Asthma and obesity are diseases of high prevalence and significant increase in the last decades. Both of them present distinct etiology, clinical phenotype, and severity. It is also known that the environmental, genetic, and inflammatory components are important in both of them.1-6

In the last 30 years, world population experienced the age of technological revolution, which provoked deep changes in lifestyle standards and feeding habits.7,8 Concomitantly, there was an improvement in hygiene and sanitary conditions and reduction of infectious diseases.9,10

Industrialization of foods, characterized by the high rates of simple carbohydrates and hydrogenated fat made these foods available to the whole population, replacing foods in natura. Besides that, the lifestyle presented a contrary movement, that is, there was a reduction of physical activity, replaced by sedentariness, and an increase in the time in front of the television, computer, and electronic games.11

In Brazil, as in various developing countries, a nutritional transition process occurred consistent with the reduction of

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This study was conducted at the Departamento de Pediatria, Setor de Pneumologia Pediátrica (Pediatrics Department – Pediatric Pneumology Department), Faculdade de Ciências Médicas (FCM), Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil.

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the prevalence of childhood underfeeding and the increase in the prevalence of overweight and obesity.\textsuperscript{7}

In Brazil, the prevalence of obesity varies according to the country region. Abrante et al., in their study, perceived that the prevalence of obesity in children was of 8.2 and 11.9\% and, in teenagers, of 6.6 and 8.4\% in Northeastern and Southeastern regions, respectively.\textsuperscript{12} Other studies conducted in the cities of São Paulo and Salvador, Brazil, found a prevalence of obesity of 10.5 and 15.8\%, respectively, in public and private school students.\textsuperscript{13,14}

Epidemiological evidence supports the theory that the relation between obesity and risk of diseases comes to existence early in the person’s life.\textsuperscript{15} It is known that when the overweight problem begins during childhood the probability of obesity is thrice enhanced in adult life, in comparison to children with normal body weight.\textsuperscript{16} There is a significant correlation between childhood obesity, hypertension, and hypercholesterolemia, these 3 conditions representing risk factors for coronary diseases in adult life.\textsuperscript{17-19}

Currently, various studies aim at establishing the relation between obesity and asthma, mainly because there was an increase in the prevalence of both in the same period. One of the aspects that were studied was if obesity could represent risk for the development of asthma.\textsuperscript{1-6} However, the physiological, immunological, mechanic, genetic, dietetic, and environmental mechanisms involved in the relation between asthma and obesity are still little known. Some questionings have been proposed: increases in prevalence of obesity and asthma are related? The inflammatory condition favored by obesity could influence in the development of asthma? The symptoms of asthma are related to the reduction of physical activity and smaller exposition to allergens, resulting in obesity?\textsuperscript{26}

The objective of this study was to review the main papers on the association of obesity and asthma and check if there is a cause-effect relation between them.

**Method**

Systematic review based in indexed data bases MEDLINE (PubMed) and Scientific Electronic Library Online (SciELO). Original articles (cross-sectional, case-control, and prospective studies) and meta-analysis published in the period that ranges from January 1998 to January 2008 were reviewed. Studies written in English, Spanish, and Portuguese were included. Keywords: obesity, body composition, asthma, childhood, inflammation and body mass index (BMI).

Twenty-five articles were reviewed, and 18 were selected according to the type of study that was used: cross-sectional study (6 articles); case-control (4 articles); prospective (6 articles); and meta-analysis (2 articles).

**Mechanisms of relation between obesity and asthma**

The excessive accumulation of body fat is defined as overweight/obesity, according to the World Health Organization.\textsuperscript{20} The criterion used in clinical practice to classify the nutritional state is the BMI, which is calculated based on the relation of weight (kg) divided by the height in square meters (kg/m\textsuperscript{2}).\textsuperscript{20,21}

The human body needs a certain amount of fat for the maintenance of physiological functions, among which are the cell membrane formation, thermal insulation, transportation, and fat-soluble vitamins storage, as well as the growth and maturation during puberty.\textsuperscript{22} The adipocytes have different functions and morphological features depending on their localization, and are responsible for secreting pro-inflammatory substances, such as IL-6, IL-1β, adiponectin, TNF-α, PC-R, and leptin.\textsuperscript{23}

The degree of obesity determines different levels of inflammation, resulting in the increase of cytokines, which participate in diverse metabolic and endocrine functions, in addition to modulating the inflammatory process and the immunological system’s response. One of the most studied inflammatory substances in obesity is leptin. It is an endogen protein whose role is related to the satiation’s control, regulation of immune response, lung function, metabolism and micronutrients regulation.\textsuperscript{23-27}

Mai et al.\textsuperscript{28} assessed the concentration of leptin found in asthmatic and overweight children. It was observed that the low serum concentration was a protection factor to the development of asthma. Therefore, the heightening of the leptin concentration could influence in the asthma’s physiopathology.

Obesity provokes mechanic effects in the lung, alters the lung volume, breathing capacity and peripheral diameter, influencing in the blood volume circulating and in the perfusion of lung ventilation.\textsuperscript{26} The decrease in the functional capacity and lung volume in obese individuals influences in the decrease in the smooth musculature movements (contraction and excitement) (Lanch hypothesis), hyper-reactivity and airways obstruction.\textsuperscript{2,23}

In a review on obesity and asthma, Beuther et al. suggest a new physiopathological mechanism in asthma, involving chemokines (leptin, IL-6, TNF-α, TGF-β, eosotin). These substances would be secreted by the macrophages, present in the visceral tissue, through the monokites (MHC-1), that would provoke effects in the atopic response, affecting the lung development, the Th1-Th2 response equilibrium, the immune response, the smooth musculature of the airways, and the increase in the bronchial hyper-responsiveness.\textsuperscript{26}

**Cross-sectional studies**

von Mutius et al.,\textsuperscript{29} in a study based on data gathered by the National Health and Nutrition Examination Survey III
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In relation to the inflammatory variables, there was no difference between the case-group and the control-group. The authors justified that the inflammatory process of the airways in asthmatic and obese children may be caused by immune mechanisms, regardless of the nitric oxide and eicosanoid levels. According to the authors, prolonged usage of IC in severe asthma increases the susceptibility to metabolic alteration, provoking weight gain, hypertension, and diabetes mellitus.

Abstracts of the cross-sectional studies about obesity and asthma are found in Table 1.

Case-control studies

A study conducted with 209 Hispanic and African American children and teenagers with ages ranging from 2 to 18 years evaluated if the weight gain in asthmatics differed from that in other children and also if the overweight was associated with the increase of asthma symptoms. Diagnostic and classification criteria for asthma severity were the ones adopted by the ATS. There was a significant association between asthma severity and overweight risk (BMI ≥ 85th). The case-group presented a relative risk (RR). By establishing BMI ≥ 95th, RR increased to 1.51 (95%CI 1.05-2.19; p = 0.03). In the control-group, 32.9 had BMI ≥ 85th and 15.3%, BMI ≥ 95th. In the case-group, 39.7% of the children had BMI ≥ 85th and 21.5%, BMI ≥ 95th, given that only 12.4% were using IC. The authors discovered that children with moderate/severe asthma and high BMI were associated with low results in the lung function test and to the bigger usage of medications for asthma control. The authors pointed that the factors that more strongly contribute to these children’s overweight are the severity of the asthma case and the limitations often imposed by the parents to the practice of physical activities. 36

Brenner et al. 37 assessed 265 asthmatic teenagers with ages ranging from 12 to 21 years and a control-group in the same age group of 482 non-asthmatics. They compared the obesity prevalence and checked if it was associated to the severity degree of asthma. The prevalence of overweight risk was of 15 to 16% in the control-group and case-group, respectively. There was no difference in the prevalence of obesity and in the severity degree of asthma (21% moderate/severe; 19% mild asthma; and 17% control). The authors concluded that obesity had no significant association with moderate/severe asthma in African-American teenagers.

Mai et al. 38 assessed the relation between the BMI and asthma and the atopic manifestations in 12-year-old children. 457 children were evaluated (case-group, 161 children, control-group, 296). An association between the high BMI and current episodes of sibilance (OR = 1.7; 95%CI 1.0-2.5). The high BMI (BMI ≥ 75th) was associated to the asthma severity, to the sibilance episodes in the last 12 months and to the presence of atopic eczema in case-children. There was no association to fever, to the increase in bronchial hyper-responsiveness and to the positive prick test.
An Italian study involving 554 asthmatic children (case) and 625 healthy children (control) evaluated the standard deviation (SD) of the BMI (±2) considering overweight/obesity BMI ≥ 2 SD. A similar percentage of children with overweight/obesity was found both in the case-group and in the control-group. It was also observed that the children and teenagers with high rates of breathing infection and who were not using IC presented BMI ≤ 2 SD. Therefore, there was no increase in the prevalence of overweight/obesity in children and teenagers who had asthma.

The abstracts of the case-control studies about obesity and asthma are found in Table 2.

**Prospective studies**

A study conducted with asthmatic children evaluated body composition by electrical bioimpedance (EB), by the dual-energy-X-ray absorptimetry (DXA) and by the skin folds.

In relation to medications, the children were divided in group 1, under usage of budesonide (400 µg/day), and group 2, under usage of fluticasone (200 µg/day), compared to control-group of asthmatic children treated with chromones and β2 agonists. After 6 months of usage, it was observed that in the case-groups (1 and 2) no alterations occurred in growth, body composition, and abdominal fat accumulation. Authors remind us that it is important to monitor height and weight in asthmatic children who use IC in low, medium, and high dosages.

Jani et al. evaluated patients younger than 18 years, analyzing if there was any difference in the BMI between those who received high dosages of IC (≥ 400 µg/day) and those who received low dosages (≤ 200 µg/day) in a time interval of 12 months. The comparison of those who received low dosages with those who received high doses showed that the latter had significant annual increase of BMI. They verified that there is a necessity of studies on the influence

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**Table 1 - Main results of cross-sectional studies on obesity and asthma**

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<tr>
<th>Authors</th>
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<tbody>
<tr>
<td>von Mutius et al.</td>
<td>7,505</td>
<td>Age group: 4-17 years.</td>
<td>- Prevalence of asthma and atopy were significant with the BMI increase.</td>
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<td>- Positive association between asthma and BMI (OR = 1.66); the same result in relation to atopy was not found.</td>
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<td>- Increase in weight results in pro-inflammatory state and contributes to elevate the airways inflammation levels.</td>
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<td>- BMI is a risk factor to the development of asthma.</td>
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<td>Schachter et al.</td>
<td>5,993</td>
<td>Age group: 7-12 years. Seven epidemiological studies.</td>
<td>- High BMI is associated to the increase in the prevalence of symptoms that may lead to asthma.</td>
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<td>- BMI increase is associated to the high prevalence of atopy diagnosis in girls, but not in boys.</td>
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<td>Antonio et al.</td>
<td>66 cases, 124 control</td>
<td>Asthma diagnosis according to the 3rd International Consensus. Age group: 4-14 years.</td>
<td>- Moderate-severe asthma alters growth due to the instability of the disease.</td>
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<td>- No obesity.</td>
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<td>- To track nutritional state and act when necessary.</td>
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<td>Leung et al.</td>
<td>92 cases, 23 control</td>
<td>Age group: 7-18 years. Asthma diagnosis and classification according to ATS and GINA, respectively. Control-group: non-asthmatic children who participated in the ISAAC.</td>
<td>- Control-group presented higher weight and height than others.</td>
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<td>- There was no difference in inflammatory markers.</td>
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<td>- Prolonged use of IC in severe asthma may contribute to metabolic altering, producing weight increase.</td>
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<tr>
<td>Hong et al.</td>
<td>24,260</td>
<td>Age group: 6-12 years.</td>
<td>- Prevalence of increase of symptoms was concomitant to the BMI in boys, but not in girls.</td>
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<td>- BMI was positively associated to sibilations and physical activity-induced sibilations.</td>
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<td>van Gent et al.</td>
<td>1,758</td>
<td>Age group: 7-10 years. Time: 2002-2005.</td>
<td>- Asthmatic children have a high BMI and low life quality.</td>
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ATS = American Thoracic Society; BMI = body mass index; GINA = Global Initiative for Asthma; IC = inhaled corticosteroid; ISAAC = International Study for Asthma and Allergies in Childhood; OR = odds ratio.
of the IC in the BMI, considering the time of usage of the medication and the severity of the asthma case.

A prospective study investigated the relation between breastfeeding and asthma, as well as the influence on the BMI. A number of 2,165 children were evaluated, and with 1,569 the prick test was used. Asthma diagnosis was done by an expert physician. It was discovered that 17% of the children had the asthma diagnosis, and 15% of the mothers also had the disease; 41% showed to have atopy in the prick test. The correlation between BMI and asthma was low, being significant only in boys. Children who had exclusive breastfeeding had a risk 4% smaller of developing asthma, mother's milk being, thus, a protective factor. Aspects of the relation between breastfeeding and asthma are still controversial, despite the numerous articles published on the theme, and they are not to be treated here.

Arend et al., in a longitudinal prospective study, observed the influence of IC usage in weight and height gain in asthmatic children seen in a public healthcare service in Porto Alegre (RS). 124 children and teenagers were included from 3 to 16 years old who received corticosteroids at least for 1 year and who had been seen for 12 months. Patients with low weight at birth (≤ 2500 g) and under mixed therapy were excluded. It was observed that there was no statistic difference between the BMI in the first evaluation and after 1 year. Comparing with the NCHS curve, patients under treatment with IC did not have height compromised.

Eijkemans et al., in a recent retrospective study, analyzed the correlation between sibilance, physical activity level and BMI. A sum of 305 children from 4 to 5 years, who had been assessed at 7 months of life, 1, 2 and 4 to 5 years, were included. There was no difference in the physical activity level among children who had had sibilation crises and the ones who had never had them. The results did not confirm that sibilations lead to overweight due to low levels of physical activity.

The abstracts of prospective study on obesity and asthma are found in Table 3.

Meta-analysis studies
Flaherman & Rutherford, in meta-analysis, showed strong evidence that the high weight in childhood increases
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Table 3 - Results of the cohort-prospective studies on obesity and asthma

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<th>Authors</th>
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<tr>
<td>Salvatoni et al.</td>
<td>26 cases</td>
<td>Age: 8.1±2.8 (3.9-14.9) years. Time: october/1996 to march/1997.</td>
<td>- Treatment with IC does not provoke growth alteration and fat accumulation.</td>
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<td>16 control</td>
<td>Moderate-severe persistent asthma diagnosis.</td>
<td>- The 6 month-period of treatment did not influence in the preschools’ body composition and growth.</td>
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<td>- In the group that received fluticasone (100 µg 2x/day) there was an increase in TBW.</td>
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<tr>
<td>Oddy et al.</td>
<td>2,165</td>
<td>Age group: seen up to 6 years old. 1,96 did the prick test. Asthma diagnosis done by physician (presence of 1 crisis/year).</td>
<td>- Increase in asthma and obesity prevalence in parallel.</td>
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<td>- 17% asthma diagnosis.</td>
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<td>- 41% of atopy according to the prick test.</td>
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<td>- Risk factors for overweight during childhood were: weight at birth and smoking during pregnancy.</td>
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<td>- Protective factor: exclusive breastfeeding reduces risk of asthma in 4%.</td>
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<td>- High BMI is a risk factor for asthma.</td>
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<td>Jani et al.</td>
<td></td>
<td>Group 1: low dosage (≤ 200 µg/day); Group 2: high dosage (≥ 400 µg/day)</td>
<td>- Regular usage of high dosages of IC is associated to significant increase in BMI, in comparison with those who received low dosages.</td>
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<td>Inclusion: patients who received fluticasone, bedometasone and budesonide. Exclusion: patients who received antileukotrienes, salmeterol (fluticasone ≥ 1.000 µg/day). Care during 12 months.</td>
<td>- Activity level and asthma severity may affect children’s BMI.</td>
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<td>- High BMI is associated with asthma prevalence increase.</td>
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<tr>
<td>Mai et al.</td>
<td>74</td>
<td>Inclusion: Birth weight ≤ 1.500 g; born between February/1987 and April/1988; leptin collection, cared until 12 years old.</td>
<td>- 16% overweight.</td>
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<td>- 16% asthmatic.</td>
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<td>- Leptin concentration reduction was a protective factor in the development of asthma in children with accelerated early growth.</td>
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<td>- Positive association between overweight and asthma in children with LBW.</td>
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<td>- Catch up could change bronchial response, reducing it.</td>
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<tr>
<td>Arend et al.</td>
<td>124</td>
<td>Age group: 3-16 years. Inclusion: using IC for at least 12 months.</td>
<td>- Age: 8.6±2.9 years.</td>
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<td>Time: October/2002-2003; 2 evaluations were done.</td>
<td>- BMI 1st: 18.2±3.16 (15.3% overweight).</td>
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<td>Exclusion: Birth weight ≤ 2.500 g, underfeeding, chronic disease and oral corticosteroid usage.</td>
<td>- BMI 2nd: 18.7±3.5 (12.1% overweight).</td>
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<td>- There was no statistic difference between evaluations.</td>
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<td>- Compared to the NCHS curve, the patients under treatment with IC for more than 12 months did not have their height compromised.</td>
</tr>
<tr>
<td>Eijkemans et al.</td>
<td>305</td>
<td>Age group: 4-5 years. Questionnaires were applied in children with ages ranging from 7 months, 1, 2 and 4-5 years. KOALA Birth Cohort Study</td>
<td>- Children who had presented sibilation in the last 12 months had a similar physical activity to those who had never had crises.</td>
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</table>

BMI = body mass index; IC = inhaled corticosteroid; LBW = low birth weight; NCHS = National Center of Health Statistics; TBW = total body water.
In another meta-analysis, Beuther & Sutherland\textsuperscript{45} observed that overweight and obesity were associated, with high OR, with the increase in asthma incidence among men and women. Seven epidemiological studies were selected after a review, including 2,006 references. The authors established the classification criterion of nutritional state as eutrophic (BMI < 25); overweight (BMI 25-29.9); and obesity (BMI ≥ 30). They found out that individuals with BMI ≥ 25 kg/m\textsuperscript{2} had a high incidence of asthma (OR = 1.51; 95%CI 1.27-1.80).

Nevertheless, some considerations were made by the authors and showed limitations in the studies included in the meta-analysis. Anthropometric data (weight, height) and related to asthma symptoms are reported by the patients and not evaluated by a medical professional, which may imply an under or overestimation of statistic data. They point that the BMI is not the best classification criterion for obesity, because it does not assess the body composition distribution (fat and thin mass) neither its localization\textsuperscript{45}

The abstracts of meta-analysis studies on obesity and asthma are found in Table 4.

**Discussion**

Both asthma and obesity increased significantly their prevalence in the last decades. Studies seek to establish relations between them: excessive weight might represent an elevated risk of developing asthma, although the physiopathological and environmental mechanism involved in this process is unknown. There is the need of determining and having more knowledge about the influence of obesity and sedentariness in the impact of asthma’s etiology, which justifies the contradictory results demonstrated by the studies.

Asthma is a multifactorial disease, involving the participation of both environmental and genetic factors. Positive family background increase the chance of an individual developing the disease in the future, which shows the relevance of genetics in the determination of this disease\textsuperscript{5,46,47}.

Environmental and life habits’ changes have a strong influence in asthma occurrence. Studies show that the environment and its changes have an influence in the genesis and physiopathological aspects of chronic diseases.

Changes in feeding habits, characterized by the imbalance in the relation among foods ingested, associated to a decrease in physical activity, contribute to the increase of prevalence of overweight/obesity and associated comorbidities (cardiovascular diseases, diabetes mellitus type 2, osteoarthritis), as occurs in asthma\textsuperscript{47}.

Persistent asthma interferes in the reduction of the patients’ life quality, increasing the likeliness of less physical activities. Asthmatic individuals are more prone to lighter activities (watching television, excessive usage of video games, computers), having a smaller caloric loss, and higher consumption of industrialized foods (rich in saturated fat, trans, simple carbohydrates, and deficient in fibers, vitamins, and minerals). The association of these factors contributes to weight gain increase\textsuperscript{6,45,47-49}.

**Table 4 - Results of meta-analysis studies on obesity and asthma**

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<tr>
<th>Authors</th>
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<th>Method</th>
<th>Conclusions</th>
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<tr>
<td>Flaherman &amp; Rutherford\textsuperscript{4}</td>
<td>12 articles (8 prospective and 4 retrospective)</td>
<td>Review at MEDLINE, from January/1996 to October/2004. BMI ≥ 85th. Ponderal index ≥ 27 kg/m\textsuperscript{3}. Birth weight ≥ 3,800 g.</td>
<td>- 4 studies verified that obese children may, in the future, develop asthma. - RR = 1.5 (95%CI 1.2-1.8) of BMI ≥ 85th was higher for children with asthma. - RR = 1.2 (95%CI 1.1-1.3) among 9 studies showed that the high birth weight increases the risk of developing asthma. - Cumulative analysis: recent studies observed that the effect of weight increase in asthma showed a negative association.</td>
</tr>
<tr>
<td>Beuther &amp; Sutherland\textsuperscript{45}</td>
<td>7 prospective studies.</td>
<td>2,006 identified references - 1,569 unified references - 95 selected according to abstract - 13 selected according to study - 7 were included. BMI &lt; 25: eutrophic (underfed were included). BMI 25-29.9: overweight. BMI ≥ 30: obesity.</td>
<td>- OR = 1.51 (95%CI 1.27-1.80) in comparing BMI ≥ 25 with asthma incidence. - OR = 1.38 (95%CI 1.17-1.62) in comparing the asthma incidence between eutrophic and overweight. - In comparing eutrophic with obese, an OR = 1.92 (95%CI 1.43-2.59) was observed.</td>
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95%CI = 95% confidence interval; BMI = body mass index; OR = odds ratio; RR = relative risk.
The association of both diseases heightens the risk of non-transmissible chronic diseases in their evolution. Brisbon et al.\textsuperscript{47} propose an organogram to better comprehend the relation of the environment’s influence in the physical activities’ practice, in obesity and asthma (Figure 1).

![Organogram showing the association between asthma and obesity](image)

**Figure 1** - Association between asthma and obesity and related factors (modified from Brisbon et al.\textsuperscript{47})

It must be understood that obesity alone cannot be the only etiology responsible for the development and increase in the asthma prevalence. Other important factors, such as genetic, immunologic, and environmental, already discussed, must be considered in the next studies. The increase of exposure to polluted environments and polluting gases emission contribute with genetic alterations, elevating the asthma prevalence.\textsuperscript{50}

A factor of extreme importance is the necessity of conducting studies with proper methods to the establishment of asthma diagnosis and treatment, since in most studies patients report asthma symptoms, with no existing classification related to its severity and to the indicated medication to the treatment, the dosage, and the time of usage.

Another point is the need of adopting different complementary anthropometric and body composition evaluation methods, in addition to the BMI (kg/m\textsuperscript{2}), as diagnostic criterion for obesity. Other parameters used present greater relevance and are complementary, such as skin folds measurement, EB, DXA, abdominal magnetic resonance, computer tomography, total body water adjustment, among others.

There is an enthusiasm in the verification that the increases in the prevalence of asthma and obesity might be the consequence of environmental changes, associated or not with other factors. Methodological rigor in future studies must seek answers to better comprehend if there are associations between asthma and obesity, or this relation is irrelevant.

**References**

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