Review paper

Obesity and asthma: risk, control and treatment

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Abstract

Asthma and obesity are currently one of the most common diseases. Observing an increase in morbidity of obesity and asthma, it can be concluded that there is a link between these diseases. But the mechanism of this relation is not well known. Due to reduced movement in patients and treatment, asthma is conducive to obesity, and obesity can exacerbate the symptoms associated with asthma. Obesity can affect bronchial hyperresponsiveness. Increasing body fat in obese people leads to systemic inflammation and elevated serum levels of many proinflammatory cytokines (e.g. leptin) and anti-inflammatory ones (e.g. adiponectin) that can have a causal relationship to bronchial asthma, but human studies are ambiguous. Obese asthmatics are characterized by a phenotype: heavier asthma, worse response to treatment and control of asthma. It has been found that in obese people, weight loss reduces the severity of asthma symptoms, so in these patients, treatment should include weight control.

Key words: body mass index, obesity, asthma, control, treatment.

Introduction

Asthma is a heterogeneous disease, usually associated with chronic respiratory tract infections, defined by respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough, varying over time and with different degrees of severity associated with variable airway obstruction [1]. Asthma is driven by different mechanisms such as mechanisms of immune regulation of allergic, inflammatory and neuroendocrine responses [2].

The incidence of asthma has increased in recent years. Causes of increased incidence of asthma are seen among environmental factors, including changes in diet and increased numbers of overweight and obese people. Bronchial asthma and obesity are one of the most important health problems in modern society, which have been termed civilization diseases. In case of asthma-related obesity, an important role play factors such as socioeconomic status, mechanic element and inflammation. Particular attention should be paid to increased intrathoracic fat deposition and fatness around the neck area. Adipose tissue causes pressure on the throat, larynx, trachea, which causes exacerbation of dyspnea as a result of the upper respiratory tract narrowing and limitation of full breathing movements, leads to reduced pulmonary vital capacity and increased respiratory resistance and the risk of asthma symptoms (Figure 1) [1–3].

The association between obesity and asthma is connected with an increased asthma severity, poorer asthma control and increased asthma exacerbation risk. In addition, obesity makes asthma difficult to diagnose. It is reported that symptoms of exercise intolerance can occur in obesity and mimic those of asthma. Furthermore, obesity is associated with an increased perception of dyspnea and this can mimic asthma [3].

Numerous epidemiological studies have shown a parallel increase in disease rates and a tendency to occur at the same time, suggesting a link between these diseases, but the mechanisms of this relation are not well known [1, 2].

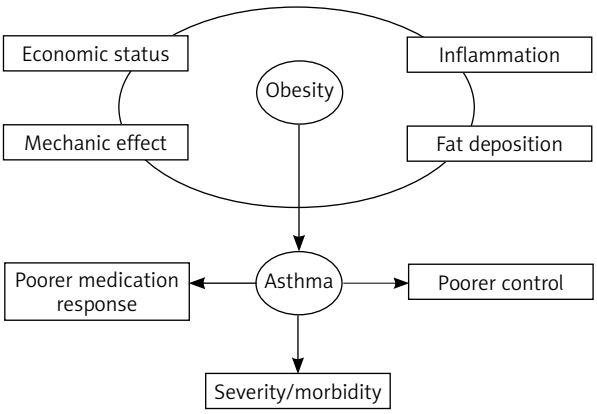

Figure 1. Asthma and obesity [1–3]

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Obesity as a risk factor of asthma: population studies

Population studies conducted over the past few years have shown an increase in the incidence of asthma in obese people compared to people with normal body weight. Data obtained during the last epidemiological studies confirmed the association between obesity and asthma, with the latter found to be a risk factor for incident asthma and affecting its severity, treatment response and control. Despite the fact that many asthma risk factors are well documented, thus far predicting the outcome of an individual patient has not been possible [2, 4]. This is mainly due to the complicated, dynamic and multifactorial elements that interact with each other throughout the development and progression of asthma. Those are socio-demographic and lifestyle factors, environmental influences, genetic and epigenetic factors [2]. Large cross-sectional and prospective studies involving adults, adolescent children throughout the world showed a relationship between high body weight and asthma (Table 1) [5–12].

Recently it has been found that not all obese asthma cases are the same. It differs between children and adults, and it can also differ by sex. In spite of the fact that there is strong evidence that obesity can raise the risk of asthma, the present study shows that in some children asthma might also increase the risk of obesity. Further studies will be necessary to determine credible mechanisms and confirm these findings [13, 14].

Active participation of mediators of adipose tissue – systemic inflammation

Research on the relationship between obesity and asthma have highlighted the mechanic, airway, and systemic inflammatory factors. Overweight affects pulmonary physiology and lung mechanics, which leads to a decrease in lung volume. Other studies have shown that systemic inflammation in overweight and obese individuals can induce asthma. It is considered that airway inflammation is more common in obese asthmatic patients since inflammation is harder to control in obese and asthmatic patients and does not respond well to glucocorticoid treatment. The reason for this is seen in pro-inflammatory adipokines and proteins released from the adipose tissue in obese individuals. It is thought that these adipokines contribute to asthma and the hypersensitivity of the airways by inducing airway inflammation or increasing existing inflammation [15].

Table 1. Population studies: obesity as a risk factor of asthma [2]

References	Population	Risk of asthma
Rajappan *et al.*, 2017	2799 mother-child pairs	Higher maternal BMI was associated with increased risks of offspring wheeze, prolonged cough and lower respiratory tract infection [5]
Forno *et al.*, 2014	10800 mother-child pairs meta-analysis of 14 studies	Maternal obesity and maternal weight gain during pregnancy were associated with 21–31% and approximately 16% increased risk of asthma in the offspring [6]
Herman *et al.*, 2016	6178 school-aged children	A higher BMI was associated with higher Rint (fat mass measures with respiratory resistance) and increased risk of wheezing in comparison with normal weight. Underweight was not associated with Rint. A higher preperitoneal fat mass, a measure of visceral abdominal fat, was associated with a higher fractional exhaled nitric oxide (FENO) [7]
Dumas *et al.*, 2016	13000 patients with maternal pregnancy overweight/ obesity	Overweight/obesity led to 19–34% increased odds of childhood asthma. In this study, boys were more likely to have nontoxic asthma and girls more likely to have atopic asthma [8]
Chih *et al.*, 2016	Over 2700 Taiwanese children	Low FEV_1/FVC was the most significant 'mediator' between central obesity and active childhood asthma [9]
Strunk *et al.*, 2015	Normal-weight children with asthma who become obese in early adulthood	The study showed worsening of FEV_1/FVC (up to 3% per each 10 kg/m^2 change in BMI), without significant changes in FVC [10]
Okubo *et al.*, 2016	100 000 hospitalizations for asthma	Obesity was associated with higher odds of mechanical ventilation and longer length of stay [11]
Myung *et al.*, 2017	Adult women aged between 40 and 65 years and elderly men aged 65 or older	Obesity was associated with self-reported asthma and pulmonary function limitations. The association was stronger when the measurement of obesity was based on body fat percentage or waist-to-height ratio, compared to BMI. There was a higher self-reported asthma risk among obese women according to the waist-to-height ratio. There was an increased risk of pulmonary function limitation with abdominal obesity, weight-to-height ratio, and obesity with regards to body fat percentage in adult women. In elderly men, obesity based on body fat percentage was associated with an increased risk of pulmonary function limitation [12]

In obese subjects there is a rise in the serum concentrations of the pro-inflammatory adipokine – leptin. Leptin is structurally related to interleukin (IL)-6 and is the main regulator of appetite. Adiponectin is synthesized and secreted by the adipocyte, regulates glucose and fatty acid metabolism, and also has anti-inflammatory properties. In patients who are obese, adipose tissue hypertrophies become infiltrated with proinflammatory macrophages [1]. The adipocytes and activated macrophages produce increased proinflammatory adipokines and cytokines that together with the decreased adiponectin levels generate "metabolic inflammation". For example, it has been shown that markers of metabolic inflammation, mainly in visceral adipose tissue, are significantly higher in obese patients with late-onset asthma compared with control subjects. While there is clear evidence of increased systemic inflammation in adults who are asthmatic-obese, there is conflicting evidence regarding systemic inflammation in children who are asthmatic-obese [1, 15].

Furthermore, limited lung function and increased airway hyper-reactivity have been reported in obese patients, and have been suggested as possible mechanisms linking obesity and asthma. In atopic asthmatic children and adolescents, obesity has been associated with increased serum leptin and tumor necrosis factor α (TNF-α) levels that enhance eosinophil chemotaxis and adhesion [16].

Regardless of that, leptin has been shown to increase the expression of pro-inflammatory cytokines TNF-α and IL-6, both associated with a Th2 phenotype, in adipocytes, macrophages, and T lymphocytes. It has consistently been shown that the mRNA levels of TNF-α and IL-6, which have been implicated in the pathogenesis of atopic dermatitis, are higher in atopic obese rats than in the non-obese ones. Leptin might also induce allergic inflammation by the activation of eosinophils via altered expression profiles of cytokines and chemokine [17].

An adipocyte-dependent regulation of the bronchial diameter, the disruption of which contributes to impaired lung function caused by abnormal body weight, has been described in mice [1]. Indeed, leptin increases the airway diameter via its cognate receptor in cholinergic neurons, in a mechanism independent of its regulation of appetite, melanocortin pathway, or sympathetic tone [1]. Asthma connected with obesity can be related to Th1 rather than Th2 inflammatory profiles; such Th1 polarization has been associated with metabolic abnormalities, worse asthma severity and control, and abnormal lung function [3, 18]. Different cytokines and adipokines associated with obesity can play a significant role, as evidenced by studies linking higher leptin and/or lower adiponectin with worse asthma severity or control [3]. Components of the innate immune system such as Th17 pathways and innate lymphoid cells have also been implicated. Like other characteristics of obese asthma, its inflammatory profile is dynamic and can differ by sex and life stage [18]. A recent study found evidence of more prominent macrophage activation among girls, with soluble CD163 (a marker of macrophage activation) associated with higher android fat deposition, lower forced expiratory volume in 1 s (FEV_1), and worse asthma control [3, 18]. A connection between asthma and obesity is seen also in the function of an appetite-modulating hormone which increases food intake and body weight – ghrelin. It has adipogenic, orexigenic, and somatotropic properties [19]. Ghrelin exerts anti-inflammatory action through the inhibition of pro-inflammatory cytokines such as tumor necrosis factor α (TNF-α), IL-1β and IL-6, which are involved in the pathogenesis of asthma [20, 21]. Tsaroucha *et al*. assessed the circulating concentrations of ghrelin in asthmatic patients and they reported that ghrelin concentrations were significantly lower in asthmatic patients compared to controls. Matsumoto *et al*. found that the level of ghrelin tended to be lower in the asthmatics than in non-asthmatic individuals. In a study by Yuksel *et al*., it was showed that the serum levels of ghrelin were decreased in asthmatic children and they suggested that ghrelin has an anti-inflammatory role in the pathogenesis of asthma by competing against IL-6 and TNF-α. Another research has shown a significant increase in the serum level of ghrelin in asthmatic patients. At this point, investigators draw attention to the anti-inflammatory effect of ghrelin which can have a noteworthy role in asthma. It has been hypothesized that this increase in ghrelin can be associated with its inhibitory role on pro-inflammatory cytokines. Because in parallel to the increase of pro-inflammatory cytokines in asthma, an increase in the level of ghrelin is expected to demonstrate its inhibitory effect on these cytokines [19, 22] (Figure 2).

Relationship between atopy and asthma caused by obesity

In comparison to children with normal weight, the risk of asthma in overweight or obese children is high-

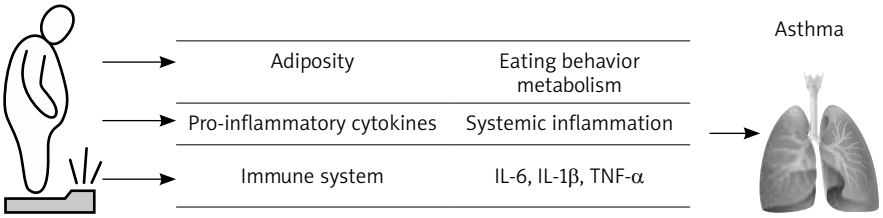


Figure 2. Relationship between obesity and asthma – systemic inflammatory factors

er, clinical symptoms of asthma are more frequent and severe, and the response to inhaled corticosteroids is worse. More and more data support the distinction of a phenotype known as "asthmatic obesity", but little is known about its characteristics. In epidemiological studies of asthma, the body mass index (BMI) was commonly used as an approximate measure of overweight or obesity. Body mass index cannot adequately characterize the relationship between overweight or obesity and complex diseases such as asthma. Among Puerto Rican people, disproportionately many asthma and overweight/obese patients are observed. US researchers have analyzed the relationship between body fat/obesity indexes, allergy indices, and measures of severity or control of asthma (i.e., lung function) in Puerto Rican asthma children living in San Juan, Puerto Rico [23, 24]. It was hypothesized that non-BMI fat mass indexes could help characterize obese asthmatics in Puerto Rican children who can have mediated atopy in relation to overweight or obesity and severity or control of asthma. Children from rural households aged 6–14 years with asthma were examined. The control group comprised children without asthma recognized by a physician. The study has shown that each index (BMI, PBF and WC) is significantly associated with asthma and is an indicator of severity or asthma control in Puerto Rican children. It has also been shown that atopy can be an important mediator of the link between obesity or obesity and asthma in this group of children. Studies underline the importance of establishing which obesity type/obesity index should be used in future studies of obesity and asthma, especially when determining phenotypes of asthmatic obesity (e.g. non-atopic vs. atopic). The results suggest that a significant percentage of the association between obesity and asthma outcomes in Puerto Rican children is due to atopy. In the study group, atopic children were a significant mediator of the effects of obesity on asthma and asthma outcomes. Future research should focus on clarifying the role of obesity and atopic sensitivity in asthma in obese children [24].

The effect of obesity on the course and effectiveness of asthma control and treatment

Obese people are not only exposed to a higher risk of developing an asthma. There are also more severe symptoms of asthma. They take more asthma medications and more often need emergency assistance than the slim ones [25].

Despite several advances in the field, there is currently no cure for asthma. Asthma associated with obesity can be resistant to oral corticosteroids. This can be due to the fact that the metabolic innate immune mechanisms and ILC3s can be unresponsive to corticosteroids. The Food and Drug Administration approved mepolizumab (anti-IL-5 monoclonal anti-body, GlaxoSmithKline) for the treatment of patients aged 12 years and older who have severe asthma with an eosinophilic phenotype [25]. Mepolizumab, which has also been studied for other diseases such as chronic obstructive pulmonary disease (COPD), hypereosinophilic syndrome, chronic rhinosinusitis with nasal polyps and eosinophilic esophagitis, is effective in reducing the number of eosinophils in the sputum and blood and in reducing asthma exacerbations and the need for treatment with systemic glucocorticosteroids [25–27]. Moreover, supervised cluster analysis of the clinical trial data showed that the subgroup cluster of patients that benefited the most from mepolizumab (cluster 4) was the one characterized by raised blood eosinophils, obesity and a mean duration of disease of 18 years [25, 28]. There are speculations that this subgroup (cluster 4) might actually include the patients described earlier with the early onset form of obesity-associated asthma [25]. Indeed, patients in this cluster of obese patients with eosinophilia had a 67% reduction in exacerbations, compared with a 16%, 53% and 35% reduction in exacerbations in clusters 1, 2 and 3, respectively, suggesting that mepolizumab can be very effective for obese patients with asthma, presumably those with the early onset asthma [25]. In patients with the late-onset form of obesity-associated asthma, it is possible that interruption of some of the metabolic pathways that leads to asthma can be effective, although no current trials are in progress targeting IL-1, IL-6, IL-17, NLRP3, M1 macrophages or ILC3s in obese patients with asthma, as far as we know. An anti-IL-17 receptor A monoclonal antibody (brodalumab, Amgen/AstraZeneca) that prevents signaling by IL-17A and IL-25, has been studied in patients with moderate-to-severe asthma [25].Though the outcomes of brodalumab-treated and placebo-treated patients were equivocal, it is possible that brodalumab can be effective only in a subpopulation of asthma patients that were not studied in this trial, for example, those with high IL-17 production, as is the case in obesity-associated asthma [25]. Further studies with brodalumab or with other pharmaceutical agents, including biologics that neutralize IL-1 or IL-6 could potentially result in new and effective therapies for obesity-associated asthma [25, 29]. Kanagalingam *et al.* reported that sinonasal disease can contribute to poor asthma control. They have investigated a connection of obesity with an increased prevalence of sinonasal disease and severity of sinonasal disease in obese asthmatics, and how this impacts asthma control. In order to determine if obesity is associated with increased severity of sinonasal disease, and/or affects response to nasal corticosteroid treatment in asthma they examined 236 adults participating in a 24-week randomized, double-masked, placebo-controlled study of nasal mometasone for the treatment of poorly controlled asthma. Obtained outcomes have shown that obesity does not affect severity of sinonasal disease in patients with asthma; the association of sinonasal disease symptoms with increased asthma severity, and markers of type 2 inflammation

are consistent across all BMI groups. Further studies are needed to investigate the response of obese patients to nasal corticosteroids [25]. To develop more effective asthma treatments we should know more about the mechanisms by which obesity impacts asthma [25].

Asthma, obesity and the microbiome

Exposure to antibiotics in early life has been associated with both obesity and asthma. However, confounding by respiratory infections can partly explain the estimated effect of antibiotics on asthma, the same is not true for the potential effects of antibiotic use on obesity. Changes in the nasal or airway microbiome have been described in asthma. In like manner, alterations in the gut microbiome have been implicated in the pathogenesis of obesity and atopic diseases (including asthma). Furthermore, aberrant responses to these microbiota have been reported to precede asthma and allergy. Probiotic supplementation has been shown to reduce the risk of atopy but not asthma [1].

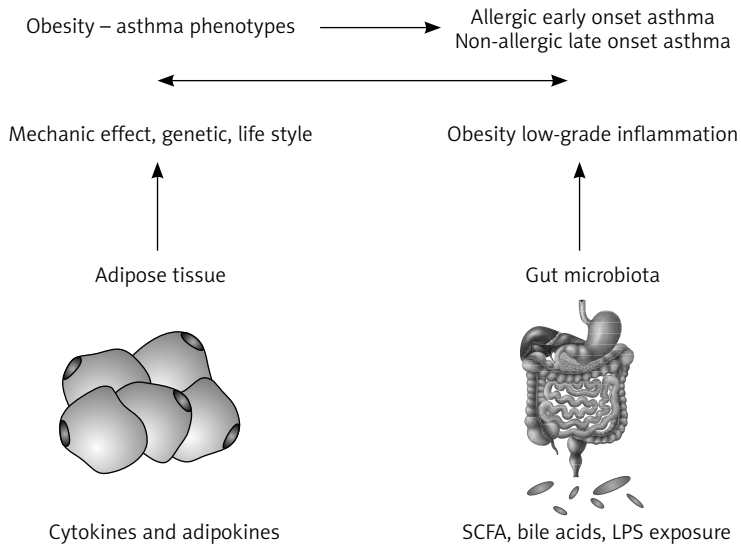
Two obesity-asthma phenotypes have been described: early-onset atopic asthma and late-onset non-atopic asthma (Figure 3). Mechanical, genetic, and lifestyle factors have been reported as mediators in these associations [1]. An important player in both these associations is adipose tissue and gut microbiota. Adipose tissue secretes adipokines and cytokines that contribute to obesity-related low-grade inflammation and might influence asthma development [1]. The gut microbiota can contribute to low-grade inflammation through the endotoxemia and the production of short-chain fatty acids (SCFAs) and bile acids. High throughput sequencing technologies have allowed us to gain a better understanding of the composition and function of the gut microbiota. Nevertheless, more studies are needed to fully understand the association between both diseases. This includes basic, animal, and clinical studies, taking into account the different asthma phenotypes and using cutting-edge techniques such as next-generation sequencing, metabolomics, and exosome studies [1].

Looking for causes of obesity development, attention was paid to the variability of intestinal microflora, depending on body weight [1, 3].

It is known that bacteria, which colonize the human digestive tract, can have a beneficial influence on the absorption of energy from food. Intestinal microflora makes better use of nutrients and more energy from nutrition. However, certain strains of bacteria can over-contribute to the synthesis of short-chain fatty acids (SCFAs), which affect the increased accumulation of fatty tissue in the body [1].

In the development of overweight and obesity, the "regulators" of appetite are also important, including leptin and ghrelin. Factors affecting their secretion can manipulate dietary behaviors, and thus influence overconsumption of energy along with diet. In a mouse study using VSL#3 multi-strain probiotic containing *Bifidobacterium breve*, *B. longum*, *B. infantis*, *Lactobacillus acidophilus*, *L. plantarum*, *L. paracasei*, *L. bulgaricus* and *Streptococcus thermophilus* has been shown to reduce appetite among the animals tested, correlated with AgRP secretion and neuropeptide Y in the hypothalamus [30].

Intestinal microflora also plays a significant role in lowering the inflammation of the organism. In Miyoshi



SCFA – short chain fatty acid, LPS – lipopolysaccaride.

Figure 3. Gut microbiota as a potential link between obesity and asthma [1]

et al. study, it was found that the supply of *Lactobacillus gasseri* SBT2055 reduced inflammation in the body and reduced the accumulation of fat in the liver – both associated with obesity and insulin resistance. Similar conclusions were obtained in the Iranian study on the correlation between intestinal microflora and IL-10 and IL-17 secretion [31]. The results showed that in subjects fed with *Lactobacillus acidophilus* La5, *Bifidobacterium* BB12 and *Lactobacillus casei* DN001, 8 weeks after ingestion, without a low-calorie diet, significant increases in IL-10 were noted and a decrease in concentration of IL-17. Among all participants, the highest increase in IL-10 was found in the BMI group of > 30 kg/m^2 compared with the non-calcium diet with low-calorie diet, indicating the influence of intestinal microflora on inflammation in obese patients. The intestinal microflora not only correlates with excessive synthesis of free fatty acids, but also it is associated with leptin secretion, prevention of type 2 diabetes and lipid disorders. This has a significant bearing on the development of obesity [32].

Recently, the number of publications on the beneficial effects of probiotics on weight reduction has increased. In the Russian study in 2013, the effects of the probiotic strain *Lactobacillus plantarum* TENSIA on the body weight of the subjects were investigated. The effects of low-calorie diet and supplementation with cheese supplemented with *L. plantarum* TENSIA on BMI and hypertension in obese patients were discussed. Each patient in the study group received 50 g/day of cheese fortified with this strain for 3 weeks. It has been shown that consumption of fortified cheese has resulted in weight, BMI, and triglyceride levels loss in obese patients. Reduction in blood pressure and blood glucose levels were similar in the study group and in the placebo group. Researchers paid attention to the effects of other protozoal strains (including *Lactobacillus gasseri* SBT2055), which can cause weight loss, and reduction in BMI, waist circumference and subcutaneous and visceral fat [33, 34].

Some of the metabolic processes in the body of obese people can also benefit from prebiotics. One study from 2015, which determined the effect of prebiotic intake (as inulin) on women's body weight, showed an increase in *Bifidobacterium longum*, *Bifidobacterium pseudocatenulatum* and *Bifidobacterium adolescentis* in the inulin group compared to the control group receiving placebo. In addition, a decrease in SCFA-acetate and propionate concentrations was observed in the feces of the women in the pre-treatment group. These women also showed better glucose tolerance and lower insulin resistance as tested by the HOMA-IR assay [35]. In addition, the effects of the use of symbiotics on weight reduction are also highlighted. In one of them, strains of *Lactobacillus rhamnosus*, *L. acidophilus*, *L. casei*, *L. bulgaricus*, *S. thermophilus*, *B. breve*, *B. longum* as probes and fructooligosaccharides (FOS) were used as prebiotics [36]. The results show that the BMI, waist-hip ratio (WHR) and waist circumference decreased. In addition, blood levels of triglycerides, total cholesterol and LDL cholesterol levels were lower in the blood tests [37].

The importance of the microbiome in both obesity and asthma is still incipient, and several aspects – such as

Table 2. Results of clinical trials of microbiome connection with asthma and obesity

References	Results
Murphy *et al*., 2014	Relationship among early antibiotic exposure and increased BMI in children, the independent effect of early-life antibiotic use in promoting increased BMI among boys [40]
Korpela *et al*., 2015	Among children who received vancomycin, a positive correlation between overall lifetime antibiotic use and BMI, as well as an increased risk of asthma, have been described, suggesting that macrolide can modify the microbiota in infants in a way that affects the weight gain associated with antibiotic use and asthma in later childhood [41]
Dzidic *et al*., 2017	Gut microbiota maintain intestinal integrity. Immunoglobulin A (IgA), the major class of antibody secreted by the gut mucosa, is an important factor. Secretory IgA (sIgA) has a decisive function in the gut through its interaction with bacterial antigens, and also because it can limit the overgrowth of selected species, thus stimulating diversity. Children with allergic manifestations present a lower proportion of IgA at 12 months of age, which can indicate impaired mucosal barrier function [42]
Orivouri *et al*., 2015	High fecal calprotectin levels, an intestinal inflammation biomarker, at 2 months of age predicted the development of asthma and atopic dermatitis at the age of 6 years [43]
Trompette *et al*., 2014	Dietary fermentable fiber and short chain fatty acid (SCFAs) can outline the immunological lung environment and influence the severity of allergic inflammation [44]
Vatanen *et al.*, 2016	Finnish and Estonian infants harbored both a greater proportion of *Bacteroides* species and enrichment in LPS biosynthesis-encoding genes when compared to Russian infants. Investigations pointed out that these Bacteroides species produced a structurally and functionally distinct form of LPS. This LPS differed from the LPS in the Russian microbiome, which was exclusively derived from *Escherichia coli*. Bacteroides LPS is structurally distinct from *Escherichia coli* LPS, and inhibits immune stimulation and the inflammatory cytokine response to *Escherichia coli* LPS in human cells. These findings suggest that differences in microbiota-derived LPS can preclude aspects of immune education [45]

Table 3. Weight loss and management of obesity [3]

References	Population	Weight loss and management of obesity
Jensen *et al*., 2013	28 obese children with asthma	Diet-induced weight loss was associated with improved asthma control and lower level of C-reactive protein (CRP) [46]
van Leeuwen *et al*., 2014	Non-controlled intervention study of 20 children	Diet-induced weight loss was associated with decreased exercise-induced bronchospasms [47]
Willeboordse *et al*., 2016	Randomized, controlled trial in 87 children	Improved asthma outcomes for both the weight loss and control groups, with some effects – such as asthma control and quality of life – being more pronounced in the intervention group (weight loss) [48]
Luna-Pech *et al*., 2014	Randomized controlled trial in 51 adolescents	A normal-calorie diet led to reductions in BMI that correlated with improved quality of life and reduced asthma exacerbations [49]
Li *et al*., 2016	Retrospective study in adults	The use of metformin among patients with diabetes and asthma was associated with improved asthma outcomes. Metformin, which acts via AMP-protein kinase (AMPK), has been shown to decrease eosinophilic airway inflammation and inhibit airway smooth muscle hypertrophy in murine models [50]

sampling-related variability [38] – need to be addressed. Nonetheless, obesity could plausibly induce or facilitate changes in the microbiome that lead to asthma. Alternatively, microbiome-host dysfunction can increase the risk of both obesity and asthma. Several factors associated with asthma, including living in an urban environment, diet, Caesarean delivery, or repeated antibiotic use, could be linked to the microbiome and – in some children – obesity. Future research in this field could yield preventive or therapeutic approaches for patients with obese asthma [39]. Results of clinical trials of microbiome connection with asthma and obesity are shown in Table 2 [40–45].

Effect of weight loss on asthma

Published studies have shown that weight loss leads to improved asthma and spirometry values in obese asthmatic patients. A significant reduction in body weight can improve asthma control, reduce symptoms and increase spirometric parameters, but without a significant reduction in eosinophilic or neutrophilic bronchitis (Table 3) [46–50].

Though obtained outcomes are promising and should prompt providers to consider managing obesity in asthma, to elucidate the effects of weight loss on 'obese asthma' in children and adults, further randomized controlled trials are needed [3]. However metformin can represent a probable adjunct therapy in obese asthma that warrants further investigation. Recent studies in adults have suggested that, whereas response to inhaled corticosteroids can be decreased, response to leukotriene antagonists can be preserved in obese patients with asthma [3].

Conclusions

Facts about the epidemiology of asthma in obese, data on its effects on hyperactivity, inflammation, as well as on the course and control of asthma, indicate significant associations between obesity and asthma and show clinical differences of asthma in obese people and people with normal BMI. However, not all patients have managed to confirm this relationship. Obesity can also be a reason for the worse response to commonly used treatment and cause difficulties in obtaining asthma control. It seems therefore that the treatment of obese patients with asthma should include weight reduction. Confirmation of the association of asthma with obesity and clarification of the relationship between the two diseases requires further research. Better standardization of methods is needed to accurately determine the relationship between obesity and asthma and determine early risk factors. Future research should focus on defining inflammatory processes, explaining weaker responses to inhaled corticosteroids and developing more effective treatment.

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Conflict of interest

The authors declare no conflict of interest.

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