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THE IMPACT OF CHILDHOOD OBESITY ON ASTHMA CONTROL

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ABSTRACT

Childhood obesity and asthma are among the most prevalent chronic diseases in the pediatric population, representing significant challenges for public health worldwide. Recent evidence suggests that obesity exerts a substantial influence on asthma control, contributing to a higher frequency of symptoms, exacerbations, and reduced responsiveness to conventional therapies. This study aimed to analyze the impact of childhood obesity on asthma control through an integrative literature review. Searches were conducted in the PubMed, LILACS, and SciELO databases using the descriptors "Pediatric Obesity," "Childhood Obesity," "Asthma," and "Disease Management." After applying the eligibility criteria, 12 studies published between 2021 and 2026 were selected for analysis. The results showed that obese children and adolescents are more likely to develop uncontrolled asthma, in addition to presenting changes in pulmonary function, a distinct inflammatory profile, increased levels of pro-inflammatory adipokines, and a higher prevalence of metabolic comorbidities. Promising biomarkers related to the obese-asthmatic phenotype and evidence of reduced responsiveness to corticosteroids were also identified. Interventions focused on weight management, nutritional education, and multidisciplinary care demonstrated improvements in metabolic and respiratory outcomes. It is concluded that obesity is an important modifier of the clinical course of pediatric asthma, requiring an integrated approach to optimize disease control and improve clinical outcomes.

Keywords: Asthma, Asthma control, Child health, Childhood obesity, respiratory diseases.

INTRODUCTION

The Childhood obesity represents one of the major public health challenges of our time, with a progressively increasing prevalence in several countries. In addition to being associated with metabolic, cardiovascular, and psychosocial alterations, excess weight during childhood has been recognized as an important risk factor for the development and worsening of respiratory diseases, particularly asthma.[1,2]

Asthma is a chronic inflammatory disease of the airways characterized by recurrent respiratory symptoms, such as dyspnea, cough, wheezing, and chest tightness, and is one of the most prevalent chronic diseases in the pediatric population. Recent evidence demonstrates that children and adolescents with obesity experience a higher frequency of asthma-related symptoms, exacerbations, and hospitalizations compared with their normal-weight counterparts, in addition to experiencing

greater difficulty achieving adequate disease control.[3,1]

The mechanisms underlying this association are complex and multifactorial. Studies indicate that obesity may induce mechanical alterations in pulmonary function, promoting airflow limitation and contributing to the development of a distinct respiratory phenotype. Furthermore, metabolic and inflammatory alterations resulting from excess adipose tissue play a fundamental role in the pathophysiology of obesity-associated asthma.[4,5]

The chronic low-grade systemic inflammation observed in obesity is mediated by pro-inflammatory adipokines and cytokines that may directly influence the immune response in the airways. Biomarkers such as leptin, adiponectin, retinol-binding protein 4 (RBP4), and plasminogen activator inhibitor-1 (PAI-1) have been associated with poorer clinical asthma control and increased inflammatory activity in children and adolescents with obesity and asthma.[5,6]

Another relevant aspect concerns therapeutic response. Children with obesity and asthma frequently exhibit reduced responsiveness to corticosteroids and greater persistence of symptoms, even with adequate pharmacological treatment. This phenomenon appears to be related to specific immunological alterations, including mechanisms of glucocorticoid resistance and changes in the inflammatory profile characteristic of the disease.[3,7]

In this context, obesity should not be considered merely a comorbidity of asthma but rather an important modifier of its clinical course. Understanding the influence of obesity on asthma control in the pediatric population is essential for developing more effective and individualized therapeutic strategies. Thus, the present study aims to analyze the scientific evidence regarding the impact of childhood obesity on asthma control, addressing the main pathophysiological mechanisms, clinical implications, and management strategies described in the recent literature.

OBJECTIVES

To analyze, through an integrative literature review, the impact of childhood obesity on asthma control in children and adolescents, investigating its influence on clinical disease control, pulmonary function, the underlying inflammatory and metabolic mechanisms, biomarkers associated with the obese-asthmatic phenotype, and the main therapeutic strategies used to manage this condition.

METHODS

This study is an integrative literature review, a method that allows for the systematic synthesis of scientific publications on a given topic and, consequently, the updating of knowledge, improvement of clinical practice, support for decision-making, identification of knowledge gaps, and suggestions for future research. Unlike a systematic review, an integrative review allows the inclusion of different study designs and the combination of theoretical and empirical data, thereby contributing to a more comprehensive understanding of the phenomenon under investigation. This method involves the following steps: identification of the topic and selection of the hypothesis or research question; literature search and establishment of study inclusion and exclusion criteria; definition and categorization of the information to be extracted from the selected studies; evaluation of the included studies; interpretation of the results; and presentation of the synthesis of knowledge.[8]

For the present review, a search was conducted in May 2026 in the National Library of Medicine (NLM/PubMed), Latin American and Caribbean Health Sciences Literature (LILACS), and Scientific Electronic Library Online (SciELO) databases. The following Health Sciences Descriptors (DeCS/

MeSH) were used: “Pediatric Obesity,” “Childhood Obesity,” “Asthma,” and “Disease Management,” combined using the Boolean operators AND and OR. To broaden the search results in the SciELO and LILACS databases, only the descriptors ((Pediatric Obesity) OR (Childhood obesity)) AND (Asthma) were used. The search strategy was restricted to studies published in Portuguese, English, or Spanish within the previous five years (2021–2026) and available as free full-text articles. A total of 149 articles were identified, of which 17 were duplicates.

Subsequently, titles and abstracts were screened to assess eligibility. Clinical trials, cross-sectional and prospective observational studies, and integrative reviews addressing the relationship between childhood obesity and asthma control, its pathophysiological and immunological mechanisms, the level of disease control, and potential therapeutic strategies were included. Studies addressing asthma and obesity exclusively in adults or in the general population, without a specific analysis of the pediatric age group, were excluded. In addition, narrative reviews, qualitative studies, and other publications unrelated to the topic and proposed objectives were excluded. Finally, after applying the described criteria, 12 articles were selected for full-text analysis. The process of article identification, screening, and selection is detailed in Figure 1, adapted from the PRISMA recommendations.[9]

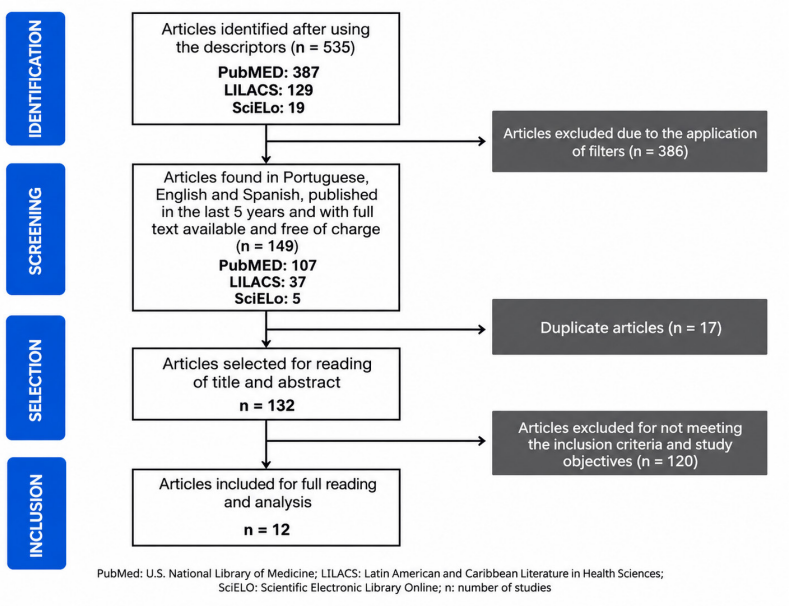

Figure 1: Flowchart of Article Selection
Source: Prepared by the authors, 2026.

RESULTS AND DISCUSSION

After applying the eligibility criteria, 13 articles published between 2021 and 2026

Were included, representing different geographical contexts, including Brazil, Cuba, China, Peru, Mexico, Greece, the United States, and Poland. The study designs included cross-sectional studies, prospective cohort studies, a case-control study, a multicenter randomized clinical trial, and a longitudinal observational study. The studies consistently examined the impact of obesity on

clinical asthma control, inflammatory profiles, pulmonary function, metabolic comorbidities, and therapeutic strategies in pediatric asthma, as summarized in Table 1.

Table 1: Characteristics of the Studies Included in the Integrative Review.

Article	Author / Year	Objective	Main Results
Phenotypic characterization of treatment-naïve childhood asthma with obesity	Maimaitiniyazi et al., 2026	To characterize the multidimensional phenotype of childhood asthma with obesity at initial diagnosis, before treatment.	Early obstructive pattern with preserved FVC; obesity as an independent predictor of the FEV_1/FVC ratio (ΔR^2 = 13.2%); T2-high phenotype in 46% of children with obesity vs. 67% of normal-weight children; 56% with dyslipidemia at diagnosis.
Asma y obesidad en pediatría	Abreu-Suárez et al., 2021	To characterize children and adolescents with asthma and obesity in terms of disease severity, control, and metabolic alterations.	88.4% had mild persistent asthma, but 65.1% had uncontrolled asthma; dyslipidemia in 53.5%; family history of asthma and obesity in 60.5%.
Relações entre asma e obesidade: análise de múltiplos fatores	Madeira et al., 2021	To compare inflammatory, clinical, and spirometric patterns between children with and without obesity, aged 6–10 years, who had asthma.	OR = 4.9 for uncontrolled asthma in children with obesity; no differences in spirometric parameters or Th1/Th2 cytokines; elevated leptin levels in groups with obesity, regardless of asthma status.
Obesity is associated with sustained symptomatology and unique inflammatory features	Fitzpatrick et al., 2022	To investigate longitudinal outcomes, response to systemic corticosteroids, and biomarkers in children with obesity and asthma over 12 months.	Poorer asthma control and more exacerbations over 12 months; inadequate response to triamcinolone; increased CRP and leptin; alterations in glutathione and arginine metabolism associated with uncontrolled asthma.
Asthma control following adenotonsillectomy	Josephson et al., 2022	To evaluate changes in asthma control among children with and without obesity following adenotonsillectomy for sleep-disordered breathing.	Normal-weight children: improvement in cACT scores at 3 and 6 months; children with obesity: improvement only at 6 months; caregiver quality of life improved in both groups.

RBP4 and PAI-1 as prognostic biomarkers	Leija-Martínez et al., 2021	To evaluate RBP4 and PAI-1 as prognostic biomarkers of obesity-related nonallergic asthma in adolescents.	Increased RBP4 and PAI-1 in nonallergic asthma with obesity; RBP4 >42.78 ng/mL: OR = 10.0; AUC = 0.741, with 90.9% specificity.
VDORA1 Randomized Clinical Trial	O'Sullivan et al., 2024	To identify a safe and effective oral vitamin D dose to achieve 25(OH)D ≥40 ng/mL in children with asthma and obesity.	Standard dose was insufficient; 78.6% achieved the target level with 50,000 IU + 8,000 IU/day; no impact on asthma control during the assessment period; no serious adverse events.
Effects of Nutritional Education and Diet	Soczewka et al., 2025	To evaluate the effects of a Mediterranean diet-based nutritional intervention on metabolic parameters and asthma control.	Reductions in cholesterol, triglycerides, and blood glucose; days with asthma symptoms decreased from 15.26 to 7.40 per month; 20.42% improvement in asthma control; reduced CRP.
Relación entre estado nutricional y severidad de asma	Llenque-Lulo; García-Gomero, 2022	To analyze the relationship between nutritional status and asthma severity in children and adolescents aged 8–17 years at a tertiary care center in Peru.	Overweight/obesity prevalence of 62.8%; 90.8% had mild asthma; no statistical association between BMI and asthma severity (p = 0.518).
Genetic polymorphisms, adipokines and adiposity in children with asthma	Machado et al., 2025	To evaluate genetic polymorphisms (FTO and TMEM18), adipokines, and adiposity in children and adolescents with asthma.	Increased leptin and decreased adiponectin in children with obesity; adiponectin >5 µg/mL associated with better pulmonary function; FTO A allele correlated with poorer spirometric parameters and lower adiponectin in the obesity group.
FKBP51 Expression in CD4+ T-Lymphocytes	Tejwani et al., 2021	To investigate dexamethasone-induced FKBP51 expression in CD4+ lymphocytes as a mechanism of corticosteroid resistance in children with obesity and asthma.	CD4+ FKBP51+ cell cluster more prevalent in children with obesity; DEX-induced FKBP51 expression associated with poorer asthma control exclusively in the obesity group (β = 1.12; p for interaction = 0.05).

Does BMI Modify the Association between Vitamin D and Pulmonary Function?	Papamichael et al., 2022	To evaluate whether BMI modifies the association between vitamin D and pulmonary function in children with mild asthma.	Vitamin D positively associated with pulmonary function only in normal-weight children; no protective effect in the overweight/obesity group; 90% had suboptimal 25(OH)D levels.

Source: Prepared by the authors, 2026.

3.2 Obesity and Clinical Asthma Control

The most consistent finding across the studies analyzed is that obesity significantly worsens clinical asthma control in children and adolescents, regardless of disease severity as formally classified by spirometry and the Global Initiative for Asthma (GINA) criteria. Abreu-Suárez et al.[1] demonstrated that although 88.4% of patients with obesity and asthma were classified as having mild persistent asthma, only 11.6% had controlled disease—65.1% had uncontrolled asthma and 23.3% had partially controlled asthma, despite the use of multiple controller medications and increasing doses of inhaled corticosteroids. This pattern was corroborated by Madeira et al.,[2] who identified a 4.9-fold higher risk of uncontrolled asthma in children with obesity compared with children without obesity (OR = 4.9; 95% CI: 1.1–22.1; p = 0.043), regardless of sex, physical activity level, and presence of atopy. The longitudinal dimension of this association was demonstrated by Fitzpatrick et al.,[3] whose 12-month follow-up revealed that children with obesity and asthma experienced a greater symptom burden, more exacerbations treated with systemic corticosteroids, and more emergency department visits throughout the study period, despite more intensive use of controller medications compared with normal-weight children.

In contrast to these consistent findings, Llenque-Lulo and García-Gomero[10] found no statistically significant association between nutritional status and asthma severity in a Peruvian sample from a specialized tertiary care center (p = 0.518), although the combined prevalence of overweight and obesity reached 62.8%. The authors themselves attributed this result to the limited sample size, heterogeneity in BMI and severity classification criteria across studies, and potential selection bias inherent in a sample drawn from a referral center with better access to subspecialists. This divergence highlights a fundamental conceptual distinction: asthma control and severity are separate categories in the GINA classification, and the absence of an association with the latter does not contradict the consistently documented impact on the former. Taken together, these findings indicate that obesity acts as a primary modifier of asthma control—and not necessarily of spirometric disease severity—which has direct clinical implications: classifying severity solely on the basis of forced expiratory volume in one second (FEV_1) may underestimate the true disease burden in children with obesity, making systematic assessment of asthma control as an independent outcome essential in this population.

3.3 Pulmonary Function: Early Obstructive Pattern, Dysanapsis, and the Role of Adipokines

The analysis of pulmonary function in children with obesity and asthma reveals a pathophysiological pattern distinct from that observed in adults. While a restrictive ventilatory pattern predominates in adults with obesity, characterized by reductions in FVC, FEV_1, and lung volumes due to the mechanical load imposed by adipose tissue on the chest wall and diaphragm, studies involving children with obesity and asthma indicate an early obstructive pattern with preserved FVC. Maimaitiniyazi et al.[4] demonstrated significant reductions in

FEV_1% (92.5 vs. 93.2; p = 0.020), the FEV_1/FVC ratio (90.3 vs. 97.0; p < 0.001), MMEF% (72.0 vs. 80.6; p = 0.005), and PEF% (91 vs. 101; p = 0.001) in children with obesity, with preserved FVC% in both groups. Multivariable analysis confirmed obesity as the strongest independent predictor of airflow limitation, explaining 13.2% of the variance in the FEV_1/FVC ratio, 5.8% in FEV_1%, and 5.3% in MMEF%, after adjustment for age, sex, and T2 inflammatory status. This pattern is consistent with the concept of developmental dysanapsis, which describes a mismatch between airway growth and lung growth, a phenomenon potentially exacerbated by obesity. Madeira et al.,[2] in turn, found no significant differences in FVC, FEV_1, the FEV_1/FVC ratio, or $FEF_{25–75}$ between children with and without obesity who had asthma, aged 6–10 years. This may reflect both the earlier stage of the obstructive process in this age group and the fact that the dissociation between symptom burden and objective pulmonary function—a phenomenon attributed to increased perception of dyspnea associated with altered chest wall mechanics, increased ventilation to meet the metabolic demands of obesity, and poor physical conditioning—may precede detectable spirometric abnormalities. This dissociation has direct clinical implications: objective assessment by spirometry is essential to avoid overtreatment in this population, particularly in the presence of pronounced symptoms that may not correspond to the actual severity of airway obstruction.

The role of adipokines in modulating pulmonary function represents an additional dimension. Machado et al.[5] demonstrated that adiponectin was significantly reduced in children and adolescents with obesity and asthma (p = 0.029), and that levels above 5 µg/mL in this group correlated with an FEV_1/FVC ratio above 80% (p = 0.035) and a positive bronchodilator test (p = 0.039), suggesting a protective role of this anti-inflammatory adipokine in pulmonary mechanics. Leptin was directly correlated with BMI (p = 0.003), and participants with greater bronchodilator responsiveness had significantly higher BMI values than nonresponders (19.4–26.84 vs. 14.55–17.16; p = 0.049). Small airway dysfunction was identified in 24.6% of participants, with an inverse correlation with BMI and the bronchodilator test, reinforcing that functional respiratory impairment in obesity-associated asthma involves both large and small airways and is mediated, in part, by adipokine-related mechanisms. Papamichael et al.[11] further reported that 90% of children with mild asthma had suboptimal 25(OH)D levels (<30 ng/mL), and that, in the normal-weight group, serum vitamin D levels were positively associated with %FVC (β = 0.49; 95% CI: 0.05–0.94; p = 0.031) and %FEV_1 (β = 0.48; p = 0.047), with normal-weight children with sufficient vitamin D levels exhibiting %FEV_1 approximately 10% higher than those with vitamin D deficiency (β = 10.43; 95% CI: 0.54–20.32; p = 0.040). In the overweight/obesity group, however, none of these associations was significant, suggesting that vitamin D sequestration in adipose tissue and resistance to the vitamin D receptor (VDR) negate its protective effect on pulmonary function in this subgroup. Taken together, these findings indicate that pulmonary function impairment in children with obesity and asthma is multifactorial—involving mechanical, adipokine-related, and metabolic mechanisms that interact with one another—and that addressing adiposity itself is a necessary, rather than merely adjunctive, measure to preserve respiratory function in this population. The most relevant methodological limitations in this group of studies include the small sample size of the overweight/obesity subgroup in Papamichael et al.[11] (n = 26) and the single-point measurement of vitamin D during a period of low cutaneous production, which may have underestimated baseline levels and compromised the accuracy of correlations with pulmonary function.

3.4 Inflammatory Profile: T2-Low Endotype, Systemic Inflammation, and Cellular Corticosteroid Resistance

Obesity substantially modifies the inflammatory endotype of childhood asthma, shifting it away from the classical Type 2 (T2) pattern toward distinct inflammatory pathways. Maimaitiniyazi et al.[4]

demonstrated that, although the prevalence of clinical atopy and total serum IgE levels were similar between children with obesity and normal-weight children, the T2-high phenotype was present in only 46% of the obesity group versus 67% of the normal-weight group (p = 0.015), accompanied by increased neutrophil levels and reduced regulatory T cells (Tregs). This dissociation between a high atopic burden and low T2 inflammation has direct diagnostic implications: conventional biomarkers such as peripheral eosinophils and fractional exhaled nitric oxide (FeNO) may underestimate actual inflammatory activity in this population, compromising risk stratification and eligibility for biological therapies targeting the T2 pathway. In partial agreement, Madeira et al.[2] observed positive skin prick tests in 80% of children with obesity and asthma and 81.8% of children without obesity and asthma, with no differences in Th1 (TNF-α, IL-6, IL-8) and Th2 (IL-4, IL-5) cytokines between groups. This suggests that, in children aged 6–10 years, the atopic component remains predominant and the endotypic shift may not yet be fully established, reinforcing the hypothesis that this inflammatory transition becomes progressively consolidated with persistent obesity throughout development.

Alongside the shift away from the T2 endotype, obesity constitutes a state of chronic low-grade systemic inflammation mediated by adipokines and macrophages in visceral adipose tissue. Fitzpatrick et al.[3] identified significantly higher plasma concentrations of C-reactive protein (CRP) and leptin in children with obesity and asthma, with a substantially increased leptin-to-adiponectin ratio, but no differences in IL-1β, IL-6, and TNF-α levels between BMI groups—a pattern distinct from that observed in adults with obesity and metabolic syndrome. Machado et al.[5] reinforced this finding by demonstrating a direct correlation between leptin and BMI (p = 0.003) and reduced adiponectin levels in children with obesity (p = 0.029), an adipokine imbalance that represents a marker of the obese-asthmatic phenotype, with implications for airway inflammation and pulmonary mechanics. Leija-Martínez et al.[6] identified M1 macrophages in visceral adipose tissue as the main source of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-17A) that sustain obesity-induced nonallergic asthma, proposing this pathway as responsible for increased levels of the adipokines RBP4 and PAI-1 in this subgroup and for progressive airway remodeling.

A specific cellular mechanism of corticosteroid resistance in children with obesity and asthma was identified by Tejwani et al.[7] Using high-dimensional flow cytometry, the authors identified a cluster of CD4+ lymphocytes coexpressing FKBP51 and Ki-67 that was more prevalent in children with obesity (2.6% vs. 1.1% in children without obesity). Following dexamethasone stimulation, FKBP51 expression in CD4+ cells was associated with poorer asthma control exclusively in the obesity group (ATAQ β = 1.12; 95% CI: 0.20–2.03; p for interaction = 0.05), with no corresponding association in the normal-weight group. FKBP51 inhibits the translocation of the glucocorticoid receptor (GR) to the nucleus and maintains it in a state of low ligand affinity, constituting a negative feedback mechanism that attenuates the response to corticosteroid therapy. This finding provides a cellular-level explanation for the clinical observation of reduced therapeutic responsiveness documented by Fitzpatrick et al.[3] and Abreu-Suárez et al.[1] Taken together, the findings of this subsection indicate that obesity-associated asthma in children is not merely a more severe variant of conventional allergic asthma but represents an immunologically distinct phenotype sustained by inflammatory pathways that are partially resistant to the mechanisms of action of conventional corticosteroids and require specific assessment and treatment strategies. The main limitations identified in this group of studies are the small sample size in Tejwani et al.[7] (n = 40, predominantly African American participants), which limits the generalizability of the immunological findings, and the absence of a healthy control group without asthma in studies evaluating inflammatory biomarkers, making it difficult to distinguish inflammation attributable to asthma from that attributable exclusively to obesity.

3.5 Metabolic Comorbidities and Their Relationship with Asthma

Metabolic comorbidities are frequent and early findings in children and adolescents with obesity and asthma, representing a pathophysiological dimension that worsens respiratory prognosis independently of BMI. Maimaitiniyazi et al.[4] demonstrated that 56% of children with obesity and asthma had at least one abnormal lipid parameter according to the NCEP 2012 criteria at initial diagnosis, before any therapeutic intervention. Abreu-Suárez et al.[1] identified a similar pattern in the Cuban population: elevated serum cholesterol in 53.5% of patients, high LDL-C in 30.2%, and low HDL-C in 23.3%, in addition to carbohydrate intolerance in 4.7% and confirmed insulin resistance in one patient. Llenque-Lulo and García-Gomero[10] documented a combined prevalence of overweight and obesity of 62.8% in their sample of Peruvian patients with asthma, demonstrating that the coexistence of these conditions is substantial across different Latin American settings, regardless of the level of development of the healthcare system.

The mechanisms through which metabolic alterations exacerbate asthma involve multiple interconnected pathways. Low HDL-C has been associated with reduced systemic anti-inflammatory capacity and worsening pulmonary function, since high-density lipoproteins exert a protective effect on the bronchial epithelium. Insulin resistance correlates with pro-inflammatory markers such as leptin and IL-6, which promote increased bronchial smooth muscle contractility and reduced airflow.[1] Machado et al.[5] identified that the A allele of the FTO gene (rs9939609) correlated, in the obesity group, with lower FEV_1/FVC ratios (46–88%; $p = 0.023$), reduced bronchodilator responsiveness ($p = 0.036$), and lower adiponectin levels ($p = 0.021$), suggesting that genetic predisposition to adiposity may amplify the metabolic impact on pulmonary function. The convergence of these findings across geographically distinct populations supports the conclusion that metabolic dysregulation is not merely a comorbidity occurring alongside obesity-associated asthma, but an active component of its pathophysiology, capable of exacerbating pulmonary impairment and bronchial hyperresponsiveness independently of the degree of obesity. This conclusion has direct clinical implications: systematic metabolic screening—including a lipid profile, fasting blood glucose, assessment of insulin resistance, and measurement of adipokine levels—should be incorporated into the care protocol for children with obesity and asthma from the time of diagnosis, not as an optional supplementary assessment, but as an integral component of management. The main limitations in this group of studies are the cross-sectional nature of most studies, which prevents establishing the temporal relationship between metabolic alterations and worsening asthma, and the heterogeneity of the diagnostic criteria used for dyslipidemia across different studies and geographical settings.

3.6 Emerging Biomarkers

The studies analyzed highlight the limitations of conventional biomarkers in the obese-asthmatic phenotype and propose emerging candidates with prognostic and therapeutic potential. Leija-Martínez et al.[6] evaluated retinol-binding protein 4 (RBP4) and plasminogen activator inhibitor-1 (PAI-1) as prognostic biomarkers of obesity-induced nonallergic asthma in adolescents. The group with nonallergic asthma and obesity exhibited significantly higher RBP4 concentrations than the group with obesity but without asthma (39.2 vs. 23.5 ng/mL; $p < 0.01$). RBP4 levels above the cutoff of 42.78 ng/mL were associated with a 10-fold higher risk of nonallergic asthma (OR = 10.0; 95% CI: 2.2–45.0; $p \leq 0.01$), with an area under the curve (AUC) of 0.741 and a specificity of 90.9%. For PAI-1, the cutoff of 12.0 ng/mL was associated with a 14-fold higher risk of nonallergic asthma (OR = 14.2; 95% CI: 1.7–119.2; $p \leq 0.01$), with an AUC of 0.699 and a sensitivity of 94.4%, but a specificity of only 45.5%, limiting its use as a standalone clinical marker. The underlying mechanism involves a higher density of M1 macrophages

in the visceral adipose tissue of individuals with obesity and asthma, which increases the production of these adipokines, sustains chronic low-grade inflammation, and promotes airway remodeling through inhibition of fibrinolysis and fibrin deposition in the bronchial epithelium.[6]

Biomarkers of different types were identified in the remaining studies, supporting the view that the obese-asthmatic phenotype has a multimodal signature. Fitzpatrick et al.[3] demonstrated, through linear discriminant analysis of 52 plasma metabolites, a distinct metabolomic profile in children with obesity and asthma: reduced concentrations of glutamine, glycine, and pyroglutamic acid and increased cystine levels, consistent with depletion of the glutathione pathway and greater systemic oxidative stress. Uncontrolled asthma at the end of 12 months was additionally associated with lower concentrations of arginine, ornithine, and glutamate, metabolites involved in nitric oxide synthesis and endothelial function. Tejwani et al.[7] identified FKBP51 expression in CD4+ lymphocytes as a cellular biomarker of corticosteroid resistance specific to the obese phenotype, with a potential therapeutic role for the selective ligand SAFit2 in experimental models. Machado et al.[5] additionally identified the A allele of the FTO gene and adiponectin levels as genetic and metabolic markers of a poorer pulmonary phenotype in individuals with obesity. Integrating these findings demonstrates that no single biomarker is sufficient to capture the complexity of the obese-asthmatic phenotype: eosinophils and FeNO underestimate inflammation; CRP and leptin reflect systemic inflammation but lack respiratory specificity; and markers such as RBP4 and FKBP51, although promising, still require validation in larger samples. This suggests that developing multimodal panels integrating adipokines, oxidative stress markers, metabolic profiles, and genetic data represents the most promising direction for risk stratification and early identification of children with obesity who are at risk of difficult-to-control asthma. The main limitations in this group of studies include the small sample sizes in biomarker studies, the wide confidence intervals of the calculated odds ratios, the cross-sectional design that precludes causal inference, and the absence of external validation studies for the identified ROC curves.

3.7 Therapeutic Strategies: Pharmacological and Nonpharmacological

Reduced responsiveness to conventional therapies is a recurrent and clinically relevant finding in studies on obesity-associated asthma. Fitzpatrick et al.[3] demonstrated that, although ACQ-6 scores improved statistically following intramuscular triamcinolone administration in children with obesity, this improvement did not reach the minimal clinically important difference. Furthermore, rescue bronchodilator use remained higher in this group during the seven days following the intervention, with significantly higher post-corticosteroid ACQ-6 scores compared with normal-weight children. Abreu-Suárez et al.[1] documented a similar pattern in the outpatient setting: most patients with obesity required multiple controller medications and progressively increasing doses of inhaled corticosteroids without achieving adequate asthma control. The cellular basis of this refractoriness was identified by Tejwani et al.,[7] who demonstrated that dexamethasone-induced FKBP51 expression in CD4+ lymphocytes—a mechanism that inhibits glucocorticoid receptor translocation to the nucleus—was associated with poorer asthma control exclusively in the obesity group ($\beta = 1.12$; p for interaction = 0.05), linking the clinical findings to the underlying immunological mechanisms.

Vitamin D has emerged as a therapeutic adjunct of interest, although with specific limitations in the context of obesity. O'Sullivan et al.[12] demonstrated that the standard dose of 600 IU/day is insufficient to achieve 25(OH)D concentrations with potential anti-inflammatory effects (≥40 ng/mL) in children with obesity and asthma—none of the participants in the standard-of-care cohort achieved this target.

A loading dose of 50,000 IU followed by 8,000 IU/day was required for 78.6% of participants to safely reach the target level, without serious adverse events. However, this increase in serum levels did not translate into a significant improvement in asthma control over the 16-week period. The findings of Papamichael et al.[11] complement this perspective by demonstrating that the protective effect of vitamin D on pulmonary function—observed in normal-weight children—was not reproduced in the overweight/obesity group, indicating that vitamin D sequestration in adipose tissue and resistance to the vitamin D receptor (VDR) due to adipose tissue dysfunction limit its effectiveness in this subgroup, even when serum levels are corrected. The convergence of these two studies allows for an important synthesis: correcting vitamin D deficiency in children with obesity and asthma is necessary to eliminate the risks associated with deficiency but is probably insufficient to exert a clinically relevant anti-inflammatory effect on the airways unless adiposity is addressed simultaneously. Future clinical trials should test this hypothesis in populations enriched for poor asthma control, with objective pulmonary function assessment and concurrent weight management interventions.

Nutritional intervention based on the Mediterranean dietary pattern demonstrated measurable benefits in both metabolic parameters and asthma control. Soczewka et al.[13] conducted a 12-month intervention involving structured nutritional education and an anti-inflammatory dietary pattern, identifying significant reductions in total cholesterol, triglycerides, and fasting blood glucose levels, increased HDL-C, reduced C-reactive protein (CRP), and a decrease in the mean number of days with asthma symptoms per month from 15.26 to 7.40 ($p < 0.05$), with an overall 20.42% improvement in disease control. Concurrent behavioral changes were documented, including increased weekly physical activity, longer sleep duration, and reduced screen time, demonstrating that structured nutritional education promotes lifestyle modifications that extend beyond dietary patterns themselves. In turn, Josephson et al.[14] demonstrated that adenotonsillectomy for the treatment of sleep-disordered breathing resulted in clinically meaningful improvements in Childhood Asthma Control Test (cACT) scores in normal-weight children at 3 and 6 months, whereas children with obesity showed improvement only at 6 months (20.00 vs. 15.00; $p = 0.048$), with caregiver quality of life improving significantly in both groups at both assessment points. The delayed surgical response in children with obesity reinforces the modifying role of adiposity in physiological recovery following therapeutic interventions. Taken together, the data on therapeutic interventions support a fundamental integrative conclusion: treatment directed exclusively at asthma, without simultaneously addressing obesity and its comorbidities—dyslipidemia, insulin resistance, sleep-disordered breathing, and systemic inflammation—is insufficient to achieve sustained disease control in this population. A multidisciplinary approach integrating pediatric pulmonology, pediatric endocrinology, nutrition, and otolaryngology when indicated is not merely an additional recommendation but an essential component of effective asthma management in children with obesity. The main limitations in this group of studies include the absence of objective spirometry in Soczewka et al.,[13] the short 16-week follow-up in the VDORA1 trial[12] involving a population with well-controlled asthma at baseline—which may have masked the potential effect of vitamin D—and the small sample size of the obesity group in Josephson et al.[14] ($n = 10$), which limits the statistical power to draw definitive conclusions regarding surgical response in this subgroup.

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