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Review Article

Asthma And Obesity: Pathophysiological Links, Clinical Impact, And Therapeutic Perspectives

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ABSTRACT

The concurrent rise of obesity and asthma worldwide has created a clinically important overlap syndrome. Obesity alters respiratory mechanics, systemic and airway inflammation, and metabolic homeostasis, producing a distinct asthma phenotype that is often less responsive to conventional anti-inflammatory therapy. Objectives are to synthesize current evidence on epidemiology, pathophysiological mechanisms, clinical consequences, and therapeutic options for patients with obesity-associated asthma, and to identify key gaps and future directions for research and practice. Methods used are Narrative, evidence-based review of primary studies, systematic reviews, and clinical guidelines focusing on human clinical research and mechanistic studies published up to 2025. Emphasis was placed on meta-analyses, randomized trials of weight-loss interventions, and major guideline updates. Obesity is associated with increased incidence of asthma and worsened control and severity in both adults and children. Mechanisms include altered lung mechanics, low-grade systemic inflammation and adipokine dysregulation (e.g., leptin, adiponectin), metabolic comorbidities (insulin resistance), and changes in the airway microenvironment. Weight reduction—through lifestyle programs, medical therapy, or bariatric surgery—consistently improves symptoms, quality of life and, in many studies, objective lung function. Obese patients often show reduced responsiveness to inhaled corticosteroids, underlining the need for phenotype-tailored strategies that incorporate weight management, treatable-trait approaches, and consideration of biologic agents when appropriate. Obesity-related asthma requires integrated management addressing excess adiposity, metabolic comorbidity, and airway disease. High-quality trials are needed to define optimal weight-loss targets, long-term outcomes, and interactions with advanced asthma therapies.

INTRODUCTION

Asthma and obesity are two chronic conditions with rising global prevalence that frequently

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coexist and interact to worsen respiratory health. Asthma affects hundreds of millions worldwide and remains an important cause of morbidity, while obesity prevalence has surged over recent decades across all age groups and regions. The epidemiologic link between increased adiposity and asthma incidence and severity has been repeatedly observed in cohort studies and meta-analyses, suggesting a dose-response relationship between body mass index (BMI) and asthma risk.

The objective of this review is to summarize current understanding of the epidemiology, mechanisms, clinical impact, and therapeutic approaches for obesity-associated asthma, integrating evidence from clinical trials, observational studies, and contemporary guideline recommendations, and to highlight priorities for clinicians and researchers.

MATERIALS AND METHODS

This is a narrative, structured review based on: (1) systematic reviews and meta-analyses; (2) randomized controlled trials and prospective cohort studies; (3) mechanistic human and translational studies; and (4) major guideline documents. Searches were performed in major biomedical databases and guideline repositories (PubMed/PMC, GINA website, WHO) up to mid-2025 to capture the most recent evidence and guideline updates. Key search terms included “obesity and asthma”, “adipokines and asthma”, “weight loss asthma randomized”, “bariatric surgery asthma outcomes”, “asthma phenotype obesity”, and “GINA 2024/2023”. For guideline and global burden information, authoritative sources such as the Global Initiative for Asthma (GINA) and World Health Organization (WHO) were used. Priority was given to meta-analyses, randomized trials, and high-quality observational cohorts when available.

RESULTS AND DISCUSSION

Epidemiology and clinical associations

Large epidemiologic studies and meta-analyses demonstrate that overweight and obesity are associated with increased incident asthma and poorer asthma control across ages and sexes. A widely cited meta-analysis found a dose-dependent increase in the odds of incident asthma with higher BMI.

Contemporary global burden assessments report hundreds of millions affected by asthma and note that comorbid obesity contributes to the overall clinical and economic burden.

Pediatric population: Childhood obesity is associated with increased risk of asthma diagnosis and with more severe disease in school-age children. Several cohort studies indicate that early-life adiposity increases later asthma risk, and obesity may alter airway growth and function during development.

Adult population: Obesity is linked to adult-onset asthma and to poor control and increased exacerbations in patients with preexisting asthma. Obese patients are more likely to be hospitalized or visit the emergency department for asthma exacerbations, and data suggest that weight gain over time increases asthma morbidity.

Clinical takeaway: Routine assessment of BMI and cardiometabolic comorbidities should be integrated into asthma care pathways; obesity is a modifiable risk factor for worse asthma outcomes.

Pathophysiology — mechanistic axes

Obesity-asthma interactions are multifactorial. They can be broadly grouped into mechanical, inflammatory/metabolic, and pharmacodynamic/phenotypic effects.



1. Mechanical effects

Excess adiposity, particularly central/abdominal fat, reduces chest wall and lung compliance, decreases functional residual capacity (FRC) and expiratory reserve volume (ERV), and increases airway closure and ventilation heterogeneity. These mechanical consequences increase dyspnea, airway hyperresponsiveness (AHR), and symptom perception, independent of allergic inflammation.

2. Systemic and airway inflammation: Adipose tissue secretes bioactive mediators (adipokines) — leptin, adiponectin, resistin — and proinflammatory cytokines (IL-6, TNF- α , CRP) which may modulate airway inflammation. Elevated leptin levels and lower adiponectin have been reported in obese asthmatic subjects; leptin has proinflammatory and immune-modulating effects that may increase airway reactivity and neutrophilic inflammation. Several focused reviews emphasize leptin and other adipokines as candidate mediators linking adiposity to airway dysfunction.

3. Metabolic dysfunction and insulin resistance

Insulin resistance and other features of metabolic syndrome associate with reduced lung function and may contribute to airway remodeling and altered immune responses. Metabolic inflammation (metaflammation) can drive systemic and airway immune shifts that differ from classic type-2 (allergic) asthma, producing a phenotype less responsive to inhaled corticosteroids.

4. Microbiome, diet, and other modifiers

Dietary patterns, gut microbiome alterations, and micronutrient status (e.g., vitamin D) influence immune development and may modify obesity–

asthma pathways, particularly in children. Environmental and behavioral factors (physical inactivity, sedentary behavior) further contribute to risk.

Integrated model: The obese asthma phenotype encompasses combined mechanical restriction, low-grade systemic inflammation (adipokine/cytokine milieu), metabolic dysregulation, and altered airway biology leading to increased symptoms, worsened control, and distinct treatment responses.

Phenotypes and treatment response

Obesity-related asthma is heterogeneous. Two commonly recognized phenotypes include:

Early-onset allergic obese asthma — obese patients with atopy and typical type-2 features but with obesity worsening control.

Late-onset non-atopic obese asthma — often adult-onset, female-predominant, with low type-2 biomarkers and neutrophilic or paucigranulocytic airway inflammation.

These phenotypes show differing responses to inhaled corticosteroids (ICS) and biologics; obese patients often have reduced steroid responsiveness, particularly in non-type-2 phenotypes, necessitating alternative or adjunctive strategies. Contemporary guidance emphasizes phenotype-directed management.

Global Initiative for Asthma - GINA

Impact of weight reduction on asthma outcomes

Interventional studies and systematic reviews show that weight loss improves asthma outcomes:

Randomized controlled trial evidence: Supervised weight-loss programs using low-energy diets with



multidisciplinary care showed significant improvements in symptoms, quality of life, and pulmonary function in obese asthmatic adults. The classic RCT by Stenius-Aarniala et al. found measurable benefits with weight reduction.

Controlled and observational studies: Several controlled trials and cohort studies report improved asthma control, fewer exacerbations, and better lung function after modest weight loss achieved through lifestyle programs. Meta-analyses of weight-loss interventions indicate consistent benefit though trial sizes are modest and heterogeneity exists.

Bariatric surgery: Bariatric surgery studies report substantial weight losses with clinically meaningful improvements in asthma control and reductions in exacerbations and healthcare utilization in many cohorts; meta-analyses and systematic reviews suggest benefit, but randomized evidence and definitive indications remain under investigation.

Clinical takeaway: Weight reduction should be considered a primary, treatable-trait strategy in obese patients with asthma. Even moderate weight loss (5–10% body weight) is associated with symptomatic and functional improvements.

Pharmacotherapy and biologics: considerations in obesity

Inhaled corticosteroids and bronchodilators

Obesity may blunt the response to ICS in some patients, particularly those with non-type-2 inflammation. Pharmacokinetic changes (e.g., altered distribution volumes) and systemic inflammation may contribute. Nevertheless, ICS remain the mainstay for patients with type-2 biomarkers or clear eosinophilic inflammation.

Biologics (anti-IgE, anti-IL-5/5R, anti-IL-4R)

Emerging evidence suggests that biologic therapies targeting type-2 inflammation remain effective in obese patients with clear type-2 disease (elevated eosinophils or FeNO), though data specific to obese subpopulations are limited. Careful phenotype assessment (biomarkers, exacerbation history) should guide biologic use.

Weight-loss pharmacotherapy

Newer anti-obesity medications (GLP-1 receptor agonists and others) produce clinically significant weight loss and may indirectly improve asthma outcomes; clinical trials evaluating asthma endpoints are limited but the potential is promising.

Integrated strategy: For obese asthmatic patients, combine evidence-based pharmacologic asthma therapy based on phenotype with aggressive weight management and treatment of comorbidities (OSA, GERD, metabolic syndrome) to optimize outcomes.

Comorbidities and special considerations

Obstructive sleep apnea (OSA), gastroesophageal reflux disease (GERD), depression, and metabolic syndrome are more prevalent in obese patients and contribute to poor asthma control and quality of life. Screening and treating these comorbidities (e.g., CPAP therapy for OSA) can yield additional symptomatic and functional gains.

Pregnancy, pediatric growth, and aging populations each present unique challenges in managing obesity-asthma interactions, requiring tailored approaches.

Gaps in knowledge and research priorities

Long-term randomized trials: More randomized controlled trials are needed comparing specific weight-loss strategies with asthma-specific



endpoints (exacerbations, lung function, biologic response).

Mechanistic biomarkers: Identification of reproducible biomarkers that predict which obese patients will benefit most from weight loss or specific pharmacotherapies.

Interaction with biologics: Studies examining interactions between obesity, metabolic status, and response to biologic agents.

Optimal weight targets: Trials to define weight-loss thresholds associated with clinically meaningful asthma improvement.

Pediatric trajectories: Longitudinal studies of childhood obesity interventions and long-term asthma outcomes.

CONCLUSION

Obesity interacts with asthma via mechanical, inflammatory, metabolic, and behavioral pathways to produce a distinct, often more severe and treatment-refractory phenotype. Weight management—through lifestyle, pharmacologic, or surgical approaches—improves asthma outcomes and should be incorporated into routine asthma care as a treatable trait. Personalized care that integrates phenotype assessment, management of comorbidities, and structured weight-loss interventions offers the best current strategy. Future research should focus on randomized trials of weight interventions with asthma endpoints, biomarker discovery to guide personalized therapy, and understanding how obesity modifies response to novel asthma treatments.

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