Annals of Medical Research
DOI: 10.5455/annalsmedres.2019.12.821 2020;27(2):695-9

Review Article

The relationship between asthma and eating disorders

Hasan Olmez[1], Nurten Arslan Isik[2]

[1]Erzincan University, Faculty of Medicine, Department of Chest Diseases, Erzincan , Turkey.
[2]Erzincan Binali Yildirim University, Faculty of Health, Department of Nursing, Erzincan, Turkey

Abstract
Obesity is a common comorbidity in asthma and obesity not only causes asthma development, but also leads to weaker asthma control and higher asthma severity. The relationship between obesity and asthma is similar to the relationship between chicken and egg. Obesity can be confusing in the diagnosis and management of asthma. Obesity in asthmatic patients causes overdiagnosis, misdiagnosis, or less diagnosis. The association of asthma and obesity has increased especially due to western type nutrition and sedentary lifestyle. Patients with obesity and asthma as a result of increased inflammatory mediators bronchoconstruction, adversely affected by lung mechanics, increased alveolar-arterial gradient, ventilation-perfusion imbalance, decreased lung volume, asthma disease and other comorbid conditions such as increased comorbid conditions, such as more frequent causes of dyspnea. They are very symptomatic, presenting more in these patients and the quality of life of these patients is worse. Another problem encountered in obese asthmatic patients is their resistance to inhaled steroids, β2-agonists and leukotrene antagonists used in asthma. Conflicting results have been obtained in studies of the effect of asthma on obesity. It is generally accepted that the development of obesity is more common in asthmatic patients due to decreased physical activity. Applying a personalized treatment plan to treat asthmatic and obese patients and applying realistic treatment methods can help the patient lose weight. In addition, obese asthmatic patients should have more symptomatic perception, obesity causes changes in lung function and obese individuals should be aware of the confusing effects of different comorbidities.

Keywords: Asthma; diet; obesity

INTRODUCTION

Asthma is a heterogeneous disease characterized by chronic airway inflammation associated with airway hypersensitivity to direct or indirect stimuli. It is defined by respiratory symptoms such as wheezing, shortness of breath, chest tightness and / or cough, and limitation of expiratory airflow. (1). The high prevalence of asthma is an important socioeconomic burden due to poor asthma control (2). Asthma affects approximately 300 million people worldwide and 250,000 asthma-related deaths have been reported. In Turkey, a study conducted between 1997 and 2004 in the prevalence of asthma was found to be 12.3% (3). Obesity is defined as a medical condition caused by excess weight or body fat that may affect human health. Body mass index (BMI) is a method used to assess whether a person has a suitable weight according to his age, gender and height. A BMI of 25 to 29.9 refers to a person being overweight, while a BMI of 30 or more indicates obesity in a person. Other factors such as waist-hip size (WHR), waist-height ratio (WtHR) ratio, and the amount and distribution of fat in the body are among the parameters that determine how healthy a person's weight is (4).

Asthma and obesity are the most common diseases currently seen worldwide. As an increase in both obesity and asthma morbidity is observed, it can be concluded that there is a connection between these diseases. However, the mechanism of this relationship is not well known (5). Recent research has shown that a hormone released from adipose tissue has a critical role in the

Received: 16.12.2019 **Accepted:** 24.02.2020 **Available online:** 10.03.2020
Corresponding Author: Nurten Arslan Isik, Erzincan Binali Yildirim University, Faculty of Health, Department of Nursing, Erzincan, Turkey **E-mail:** nurtenarslanisik1@gmail.com

development of obesity-related asthma and may be a target for future treatments for the disease. New treatments are needed for obesity-related asthma because these patients respond less to current treatments (6). Obesity is associated with increased expiration of the 5-lipoxygenase pathway and increased leukoterin production has been observed in obese asthmatic patients. In particular, cysteinyl leukotreins should be investigated in obese asthmatic patients (7). Several inflammatory pathways have been described that affect asthma in obesity. Pathways containing natural lymphoid cells (ILC) type 2 (ILC-2), surfactant protein-A, cell division control protein (CDC) 42, IL-6, IL-17 and IL-33 probably cause inflammatory effects in obese asthmatic patients (8). It has been shown that high-fat diet may exacerbate airway inflammation through the mechanism containing ILC2 and ILC3 (9). In a study, it was shown that obesity in childhood is associated with high circulating ILC3 frequency and inflammation in asthma through high expiration of IL-22 and IL-17A, and RORC gene mRNA (10). In a study, obese asthmatic subjects showed an increase in myosin light chain (MLC) phosphorylation in airway smooth muscle (ASM) cells and hypersensitivity to agonists in ASM cell contraction and increased agonist-induced calcium mobilization (11). Another study, an association was found between DNA methylation and BMI measured in the peripheral blood of adult patients and it was stated that there might be a correlation between BMI change and late-onset asthma development in non-atopic adults (12). Visceral obesity is known to be a more important risk factor in cardiovascular diseases than general obesity. Although the relationship between visceral obesity and cardiovascular diseases is well known, this relationship is not fully understood in asthmatic patients. In a study, it was stated that epicardial adipose tissue did not increase in asthmatic patients compared to normal population and visceral obesity could not be an important risk factor for asthma (13). However, another study showed that anthropometric measurements were associated with increased asthma symptoms and poor asthma control, especially among women. Regardless of gender, abdominal visceral fat layer was associated with decreased quality of life, more prominent than other obesity indices. This is due to the lower FEV1, higher rate of gastroesophageal reflux disease caused by abdominal visceral fat, and more frequent depression in these patients. Therefore, visceral adiposity may have more clinical effects on asthma symptoms than other obesity indices (14). Obesity may affect bronchial hypersensitivity. Increased body fat in obese individuals leads to elevated serum levels of many proinflammatory cytokines (eg, leptin) and anti-inflammatory (eg, adiponectin) cytokines that may have a causal relationship with systemic inflammation and bronchial asthma, but human studies are uncertain. (18). Body composition, asthma control and IL-1β, IL-4, -IL13, leptin and adiponectin levels of obese asthmatic patients were found to be significantly different when compared with fat-free normal-weight asthma patients (15). It is important to note the effects of obesity and insulin resistance (IR) in asthmatic patients because these may affect the patient's symptoms (16). Waist height ratio (WHtR) and IR affect lung function in overweight / obese asthmatic adults. IR also changes the relationship between excessive adiposity and respiratory function in adults with asthma (17). IR resistance is a factor affecting the relationship between asthma and obesity and this effect is independent of other components of the metabolic syndrome such as hyperlipidemia, hypertension, hyperglycemia and systemic inflammation (20). IR and low HDL levels may be associated with pulmonary morbidity. Evidence has been presented regarding its effect on IR airway smooth muscle and bronchial hyperactivity (16). Th1 polarization and monocyte activation may be correlated with metabolic abnormalities in patients with asthma and obesity. Th1 polarization is likely to be mediated by IR and monocyte activation may be caused by increased BMI (18). IR also affects pulmonary function in the non-obese population (17). However, contrary to these results obtained in a study, 1662 children (3 to 11 years) and 12.179 adolescents (12 to 19 years) participated in another study in children or adolescents with serum lipids or IR found no relationship between asthma (19). In previous studies, the increase in BMI and asthma were found to be high especially in nonallergic female patients over the age of 18 (20). In obese asthmatic patients, especially in girls, fat mass is infiltrated by activated macrophages and mast cells. In a study, serum soluble CD163 levels were found to be high in obese girls. It has been shown that having sex-specific macrophage activation in obese children with asthma adversely affects respiratory function and asthma control (21). In another study, it has been shown that sex hormones affect systemic inflammation and have a lower sputum neutrophil rate in women using oral contraceptives (OCS) (22). Obese adults with asthma are more likely to develop dynamic hyperinflation and expiratory flow restriction than non-obese asthmatics (23). Although waist circumference is associated with restrictive effects on basal lung function, increased BMI has been shown to have a more pronounced effect on bronchoconstriction rather than waist circumference (24). In obese asthmatic patients, lung volumes change, airway obstruction increases, and gas exchange is affected. In addition, increased lung blood volume, increased chest wall fat infiltration and compression of the rib cage with fatty soft tissue decrease compliance. Functional residual capacity, expiratory volume is affected too much; total lung capacity, forced vital capacity is less affected (25). Early closure of the airways is common in these patients. Airway resistance increases and bronchial obstruction develops due to decreased lung volumes, reduced airway diameter, fatty infiltration of the chest wall, and modified actin myosin bridges in the bronchial smooth muscle. Early closure of the airways during expiration causes air trapping. This is why the residual volume is preserved (26). In obese asthmatic patients, alveolar-arterial gradient increases while arterial oxygen pressure does not change. Obesity causes a decrease in ventilation and obstruction of small

airways in asthmatic patients, thus facilitating the development of ventilation perfusion imbalance (27). As a result, dyspnea and exercise intolerance occur (28). The role of obesity in adult asthma is well known. Results from previous studies show that overweight and obesity have an independent causal detrimental effect, whereas decreased physical activity does not have an independent causal effect on asthma development (29). Decreased physical activity is often seen in children with asthma due to uncontrolled asthma symptoms and incorrect parental belief. Clinicians working in the field of allergy are aware of the evidence supporting the benefits of physical activity for patients with asthma. Since exercise performance of children with asthma under control is not different from healthy controls, no exercise limitation is appropriate (16). Obesity is the two common health problems worldwide with a prevalence of 13% and chronic cough 9.6%. The critical role of obesity in the development and progression of many respiratory diseases is emphasized. According to the results of epidemiological studies, obesity, especially abdominal obesity, may also be associated with chronic cough. Chronic cough is more severe in obese patients than in normal weight patients. Treatment of chronic cough can be more difficult in obese patients than in non-obese patients. Obstructive sleep apnea and diabetes can lead to chronic cough and should be considered in obese patients with chronic cough (30).

As a result of the studies, it was found that BMI increase was not associated with increased risk of respiratory infection in children or adults (31). Depression symptoms are increased in asthma patients with poor control and are closely related to obesity. It is a fact that asthma control deteriorates as depression increases (32). In a study, obese patients experienced more sleep disturbances and gastroesophageal reflux complaints and had higher cytokine levels (33). While the presence of high fat may cause asthma, the effect of asthma on fat accumulation seems to be less (58). Exercise is part of a strategy to achieve good asthma control in childhood. However, we should optimize asthma treatment before starting the exercise program (16). The most accurate approach seems to be low-calorie diet and physical activity. Weight loss leads to a reduction in symptoms and an improvement in quality of life in asthma control (23).

In a study, dietary restrictions, exercise training and cognitive behavioral therapy with weight loss in individuals with obesity and asthma for 8 weeks to 18 months have been shown to improve asthma outcomes (34). Weight loss of patients provides decrease in inflammatory mediators and increase in antieflamatory mediators (35). Response to long-acting b2-agonists, inhaled corticosteroids, leukotrein antoginists is less in obese asthmatic patients than in normal weight patients (36,37). Since neutrophilic infiltration is more dominant in obesity-induced asthma, the effect of anti IgE and antieosinophilic therapy is limited. The treatment of other comorbidities caused by obesity may be helpful in the treatment of asthma. Weight loss appears to improve the breathing mechanism during exercise. It shows that moderate weight loss may improve dynamic hyperinflation in obese patients with asthma due to decreased abdominal fat. In addition, at least 5% weight reduction has been shown to delay the onset of dynamic hyperiflation and expiratory flow limitation, as well as to improve asthma quality of life and asthma control (23). Omalizumab is recommended in patients with severe allergic persistent asthma. Omalizumab has been shown to significantly improve asthma control and reduce salvage and asthma exacerbations in the entire population. The use of omalizumab in obese asthmatic patients has been shown to significantly improve lung function (38). Obesity and hypoventilation syndrome is common in patients with obesity and asthma; CPAP treatment may also be helpful in controlling asthma in these patients (39). Epigallocatechin-3-gallate (EGCG) has been shown in obese animal experiments to reduce airway inflammation and restore oxidant stress markers to normal. It has been recommended to investigate for treatment in asthmatic patients with obesity (40). Neutrophil elastase inhibitors (NEI) have been shown to promote the release of various antioxidant factors, increase the activity of antioxidant enzymes and improve the symptoms of obese asthmatic mice (41). In fact, asthma and gastro-oesophageal reflux diseases, which are considered as key factors in the onset of chronic cough, are characterized by more severe symptoms in obese patients. There are no data on the effect of inhaled therapies in obese subjects with cough variant asthma. It has been suggested that weight loss may have a beneficial effect on chronic cough (30).

CONCLUSIONS

Asthma and obesity are two common diseases worldwide. Obesity affects lung mechanics, particularly visceral obesity, and causes an increase in inflammatory mediators released from adipose tissue. Comorbid conditions are more common in obese asthmatic patients. For these reasons, obese asthmatic patients are clinically more symptomatic and have poor asthma control. It has been shown that when obese asthma patients lose weight, their symptoms decrease and quality of life increases. In addition, obesity may lead to overdiagnosis, misdiagnosis or underdiagnosis in asthma patients. Asthma, on the other hand, can cause obesity due to poor control and lack of physical movement and exercise. When planning treatment of obese asthma patients, all these factors should be considered and treatment should be personalized.

Hasan Olmez ORCID: 0000-0002-5192-6264
Nurten Arslan Isik ORCID: 0000-0002-5192-6263

REFERENCES

1. Global Initiative for Asthma [GINA]. Global strategy for asthma management and prevention [Update2015]. Avaliable.from:http://www.ginasthma.org/local/uploads/files/GINA_Report_2015.pdf.

2. Solé D, Aranda CS, Wandalsen GF. Asthma: epidemiology of disease control in Latin America – short review. Asthma Res Pract [Internet] 2017;3:4.
3. Turkish Thoracic Society Asthma Diagnosis and Treatment Guide, 2010, http://toraks.org.tr/uploadFiles/book/file/410201117401
4. What is obesity and what causes it? Last reviewedFri 2 Nov 2018 By Yvette BrazierReviewed by Katherine Marengo LDN, RD.
5. Marko M, Pawliczak R. Obesity and asthma: risk, control and treatment. Adv Dermatology Allergol [Internet]. 2018;35:563-71.
6. Aeberli I, Beljean N, Lehmann R, l'Allemand D, Spinas GA, Zimmermann MB. The increase of fatty acid-binding protein aP2 in overweight and obese children: interactions with dietary fat and impact on measures of subclinical inflammation. Int J Obes [Internet]. 2008;32:1513-20.
7. Yadav U, medicine SS-C molecular, 2015 undefined. Cysteinyl leukotrienes (CysLTs): role in obesity-induced asthma. ingentaconnect.com [Internet]. [cited 2019 Apr 13]; Available from: https://www.ingentaconnect.com/content/ben/cmm/2015/00000015/00000007/art00003
8. Grace J, Mohan A, pulmonary NL-C opinion in, 2019 undefined. Obesity and adult asthma: diagnostic and management challenges. journals.lww.com [Internet]. [cited 2019 Apr 13]; Available from: https://journals.lww.com/co-pulmonarymedicine/Fulltext/2019/01000/Obesity_and_adult_asthma___diagnostic_and.7.aspx
9. Everaere L, Ait-Yahia S, Molendi-Coste O, Vorng H, Quemener S, LeVu P, et al. Innate lymphoid cells contribute to allergic airway disease exacerbation by obesity. J Allergy Clin Immunol [Internet]. 2016;138:1309-18.
10. Wu Y, Yue J, Wu J, et al. Obesity May Provide Pro-ILC3 Development Inflammatory Environment in Asthmatic Children. J Immunol Res [Internet] 2018:1-9.
11. Orfanos S, Jude J, Deeney BT, et al. Obesity increases airway smooth muscle responses to contractile agonists. Am J Physiol Cell Mol Physiol [Internet]. 2018;315:673-81.
12. Jeong A, Imboden M, Ghantous A, … AN-I journal of, 2019 undefined. DNA Methylation in Inflammatory Pathways Modifies the Association between BMI and Adult-Onset Non-Atopic Asthma. mdpi.com [Internet]. [cited 2019 Apr 13]; Available from: https://www.mdpi.com/1660-4601/16/4/600
13. Yılmaz HEB, Yılmaz M, Şen N, et al. Investigation of the Relationship between Asthma and Visceral Obesity by Epicardial Fat Thickness Measurement. Turkish Thorac J [Internet]. 2019;20(1):1-5.
14. Goudarzi H, Konno S, Kimura H, … HM-TJ of A, 2018 undefined. Impact of Abdominal Visceral Adiposity on Adult Asthma Symptoms. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S2213219818307414
15. Liu Y, Zheng J, Zhang HP, et al. Obesity-Associated Metabolic Signatures Correlate to Clinical and Inflammatory Profiles of Asthma: A Pilot Study. Allergy Asthma Immunol Res [Internet]. 2018;10:628.
16. Milanese M, Giudice E del, immunopathologia DP-A et, 2018 undefined. Asthma, exercise and metabolic dysregulation in paediatrics. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S0301054618300818
17. Sadeghimakki R, McCarthy HD. Interactive effects of adiposity and insulin resistance on the impaired lung function in asthmatic adults: cross-sectional analysis of NHANES data. Ann Hum Biol [Internet] 2019;1-7.
18. Rastogi D, Fraser S, Oh J, et al. Inflammation, Metabolic Dysregulation, and Pulmonary Function among Obese Urban Adolescents with Asthma. Am J Respir Crit Care Med [Internet] 2015;191:149-60.
19. Lu M, Wu B, Qiao R, et al.YD-J of clinical, 2019 undefined. No Associations Between Serum Lipid Levels or HOMA-IR and Asthma in Children and Adolescents: a NHANES Analysis. europepmc.org [Internet]. [cited 2019 Apr 13]; Available from: https://europepmc.org/abstract/med/30759963
20. Barranco P, Delgado J, Sastre J, et al. Obesity is not Associated with Mild Asthma Diagnosis in a Population of Spanish Adults. J Asthma [Internet]. 2009;46:867-71.
21. Periyalil H, Wood L.HS-E, 2015 undefined. Macrophage activation, age and sex effects of immunometabolism in obese asthma. Eur Respir Soc [Internet]. [cited 2019 Apr 13]; Available from: https://erj.ersjournals.com/content/45/2/388.short
22. Scott HA, Gibson PG, Garg ML, et al. Sex hormones and systemic inflammation are modulators of the obese-asthma phenotype. Allergy [Internet] 2018 ;71:1037-47.
23. Grandi Silva A, Duarte Freitas P, Ferreira PG, Stelmach R, Carvalho-Pinto RM, Salge JM, et al. Effects of weight loss on dynamic hyperinflation in obese women asthmatics. J Appl Physiol [Internet]. 2019;126:413-21.
24. Peters U, Subramanian M, Chapman DG et al. BMI but not central obesity predisposes to airway closure during bronchoconstriction. Respirology [Internet]. 2019 Jan 29 [cited 2019 Apr 13]; Available from: http://doi.wiley.com/10.1111/resp.13478
25. Sin D, Thorax ES-, 2008 undefined. Obesity and the lung: 4• Obesity and asthma. thorax.bmj.com [Internet]. [cited 2019 Apr 13]; Available from: https://thorax.bmj.com/content/63/11/1018.short
26. Ferretti A, Giampiccolo P, Cavalli A. Chest JM-E-, 2001 undefined. Expiratory flow limitation and orthopnea in massively obese subjects. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S0012369215395982

27. Brazzale DJ, Pretto JJ, Schachter LM. Optimizing respiratory function assessments to elucidate the impact of obesity on respiratory health. Respirology [Internet]. 2015;20:715-21.
28. Scott HA, Wood LG, Gibson PG. Role of Obesity in Asthma: Mechanisms and Management Strategies. Curr Allergy Asthma Rep [Internet]. 2017;17:53.
29. Bédard A, Serra I, Dumas O, et al. Time-Dependent Associations Between Body Composition, Physical Activity, and Current Asthma in Women: A Marginal Structural Modeling Analysis. Am J Epidemiol [Internet] 2017;186:21-8.
30. Guilleminault L. Chronic cough and obesity. Pulm Pharmacol Ther [Internet]. 2019;55:84-8.
31. Tang M, Henderson R, Holbrook J. LQ-TJ of A, 2019 undefined. Does Obesity Increase Respiratory Tract Infections in Patients with Asthma? Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S221321981830610X
32. Kapadia S, Wei C, Bartlett S, Lang J. RW-R, 2014 undefined. Obesity and symptoms of depression contribute independently to the poor asthma control of obesity. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S0954611114001991
33. Dixon AE, Shade DM, Cohen RI, Skloot GS, Holbrook JT, Smith LJ, et al. Effect of Obesity on Clinical Presentation and Response to Treatment in Asthma. J Asthma [Internet] 2006;43:553-8.
34. Okoniewski W, Lu KD, Forno E. Weight Loss for Children and Adults with Obesity and Asthma: A Systematic Review of Randomized Controlled Trials. Ann Am Thorac Soc [Internet]. 2019 Jan 3 [cited 2019 Apr 13];AnnalsATS.201810-651SR. Available from: https://www.atsjournals.org/doi/10.1513/AnnalsATS.201810-651SR
35. Baltieri L, Cazzo E, Souza A de. SA-R, 2018 undefined. Influence of weight loss on pulmonary function and levels of adipokines among asthmatic individuals with obesity: One-year follow-up. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S0954611118303238
36. Schatz M, Allergy CCJ-A of, Immunology A&, 2003 undefined. The relationship of sex to asthma prevalence, health care utilization, and medications in a large managed care organization. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S1081120610615335
37. Mannino DM, Homa DM, Akinbami LJ, et al. Surveillance for asthma--United States, 1980-1999. MMWR Surveill Summ [Internet]. 2002 Mar 29 [cited 2018;51:1-13.
38. Oliveira M, Vieira M, Coutinho D, et al, Pulmonology IP-, 2019 undefined. Severe asthma in obese patients: Improvement of lung function after treatment with omalizumab. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S2531043718300369
39. Pawelec-Winiarz M, (Warsaw AK-..., 1960) P, 2018 undefined. Coexistence of asthma and the obesity-hypoventilation syndrome. europepmc.org [Internet]. [cited 2019 Apr 13]; Available from: https://europepmc.org/abstract/med/30176621
40. André D, Horimoto C. MC-I, 2018 undefined. Epigallocatechin-3-gallate protects against the exacerbation of allergic eosinophilic inflammation associated with obesity in mice. Elsevier [Internet]. [cited 2019 Apr 13]; Available from: https://www.sciencedirect.com/science/article/pii/S1567576918302790
41. Zheng J, Zhang G, Li J. For HB-E review, 2019 undefined. Neutrophil elastase inhibitor suppresses oxidative stress in obese asthmatic rats by activating Keap1/Nrf2 signaling pathway. europeanreview.org [Internet]. [cited 2019 Apr 13]; Available from: https://www.europeanreview.org/wp/wp-content/uploads/361-369.pdf.