

# Asthma exacerbations and body mass index in children and adolescents: experience from a tertiary care center

Danish Abdul Aziz,<sup>1</sup> Rameen Ata Bajwa,<sup>2</sup> Werdah Viquar,<sup>2</sup> Fatima Siddiqui,<sup>3</sup> Aiza Abbas<sup>2</sup>

<sup>1</sup>Department of Pediatrics and Child Health, Aga Khan University Hospital, Karachi; <sup>2</sup>Medical College, Aga Khan University, Karachi;

<sup>3</sup>Dr. Ruth K.M Pfau Civil Hospital, Karachi, Pakistan

Correspondence: Danish Abdul Aziz, Department of Pediatrics and Child Health, Aga Khan University Hospital, Stadium Road, Karachi, 74800, Pakistan.

Tel.: 0092-333-2345673.

E-mail: drdanishaziz@gmail.com

Key words: body mass index, asthma exacerbation, lung volumes, obesity.

Contributions: DA, RB, conception and design of the study; WV, AA, data collection; FS, DA, analysis and interpretation of data; DA, RB, AA, drafting of the work and critical revision for important intellectual content. All authors approved the final version for publication and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interest: the authors declare they have no competing interests, and all authors confirm accuracy.

Ethics approval and consent to participate: approval was received by the Ethics Review Committee at Aga Khan University Hospital. All mentioned ethical aspects and related consents were taken into considerations during the conduct of this study.

Patient consent for publication: not applicable.

Funding: none.

Availability of data and materials: data and materials are available from the corresponding author upon request.

Acknowledgments: IT and medical record Departments, Aga Khan University Hospital, Karachi, Pakistan.

Received: 13 March 2023.

Accepted: 8 June 2023.

Early view: 27 June 2023.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

©Copyright: the Author(s), 2023

Licensee PAGEPress, Italy

Monaldi Archives for Chest Disease 2024; 94:2581

doi: 10.4081/monaldi.2023.2581

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial International License (CC BY-NC 4.0) which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

## Abstract

The prevalence and incidence of asthma continue to rise globally. Obesity has been identified as a potential risk factor for asthma exacerbations. The association between body mass index (BMI) and asthma is not well studied in some regions. This study aims to investigate the impact of BMI on pediatric asthmatic patients. This retrospective study was conducted at the Aga Khan University Hospital from 2019 to 2022. Children and adolescents with asthma exacerbations were included. The patients were classified into four groups based on their BMI: underweight, healthy weight, overweight, and obese. The demographic characteristics, medications used, predicted forced expiratory volume in 1 second (FEV<sub>1</sub>) measurements, asthma exacerbations per year, length of stay per admission, and the number of patients requiring high dependency unit (HDU) care were recorded and analyzed. Our results demonstrated that patients in the healthy weight category had the highest percentage of FEV<sub>1</sub> (91.46±8.58) and FEV<sub>1</sub>/forced vital capacity (FVC) (85.75±9.23) (p<0.001). The study found a significant difference in the average number of asthma exacerbations per year between the four groups. Obese patients had the highest number of episodes (3.22±0.94), followed by the underweight group (2.42±0.59) (p<0.01). The length of stay per admission was significantly shorter for patients with a healthy weight (2.0±0.81), and there was a statistically significant difference observed in the number of patients requiring HDU care among the four groups, as well as in the average length of stay at the HDU (p<0.001). Elevated BMI is related to an increased number of annual asthma exacerbations, a low FEV<sub>1</sub> and FEV<sub>1</sub>/FVC, an increased length of stay at admission, and an increased stay in the HDU.

## Introduction

Asthma prevalence and incidence continue to rise in children worldwide [1]. While there are many factors that contribute to the severity of asthma exacerbations, there is an increasing interest in the association between elevated body mass index (BMI) and asthma exacerbations [2,3]. There are various theories of how obesity and asthma are related, with Shan *et al.* reporting a bi-directional relationship between the two during childhood and adolescence [4]. Obesity is associated with chronic low-grade systemic inflammation as it increases the risk of atopy and T-helper type 2 responses [1,5]. Adipose tissue is thought to regulate systemic inflammation through adipokines, thus implying that obesity can increase the risk of developing asthma as well as make it difficult to manage [5]. Obese children with asthma are seen to have worse lung function,

greater severity and poorer control of asthmatic symptoms, and frequent asthma exacerbations when compared to children of healthy weight [6-8]. The duration of obesity is also seen to negatively impact lung function tests; a study done in 2012 reported an increased duration of obesity as a predictor of lower function tests [9]. Furthermore, children with obesity show a decreased responsiveness to inhaled corticosteroids (ICS) and a lower asthma-related quality of life [6,8,10]. The relationship between low body weight and asthma has not been well established; however, the association of low body weight with an increased risk of developing asthma has been seen in men [11]. Furthermore, being underweight and overweight has been associated with an increased risk of developing asthma [12]. This relationship between asthma and obesity can be explained by various different aspects, including, but not limited to, the duration of obesity [9], the presence of significant co-morbidities, common in-utero conditions, and common predisposing dietary factors [13]. Furthermore, there is significant evidence that obesity and asthma may share the same genetic risk factors [14,15].

The association between BMI and asthma is not well studied in our region. Therefore, we aim to explore the impact of BMI in pediatric asthmatic patients and study its impact on asthma exacerbations, length of stay (LOS) in the hospital for each exacerbation, admission in the high dependency unit (HDU), and the LOS in the HDU. We theorize that an increasing BMI is associated with a higher rate of asthma exacerbations among pediatric patients. The objective of this study is to demonstrate the association between BMI and asthma exacerbations in children and adolescents with asthma.

## Materials and Methods

A retrospective study was conducted at the Aga Khan University Hospital, Karachi, Pakistan, from January 2019 to December 2022. Children and adolescents aged 6-18 years who were diagnosed and admitted with acute asthma exacerbations were included. BMI was documented for every patient, and their data for the past year were analyzed for baseline forced expiratory volume in 1 second (FEV<sub>1</sub>) and FEV<sub>1</sub>/forced vital capacity (FVC) ratio, number of asthma exacerbations, mean LOS per admission, HDU admission, and LOS at HDU (also known as the special care unit, which is a level below the intensive care unit). Patients were categorized into four groups: i) underweight with a BMI less than the 5<sup>th</sup> percentile; ii) healthy weight with a BMI between the 5<sup>th</sup> percentile and less than the 85<sup>th</sup> percentile; iii) overweight with a BMI between the 85<sup>th</sup> percentile and less than the 95<sup>th</sup> percentile; iv) obese with a BMI 95<sup>th</sup> percentile or greater. The World Health Organization guidelines were used to categorize patients according to BMI. BMI is defined as body mass in kilogram (kg) divided by the square of the body height in meters (m<sup>2</sup>) and is expressed in units of kg/m<sup>2</sup> [16]. These values were then plotted on BMI centile charts published by the Centers for Disease Control and Prevention to categorize the patients into four different groups [17].

The diagnosis of asthma was done according to the Global Initiative for Asthma (GINA) guidelines: i) identifying characteristic episodic respiratory symptoms, including wheezing, shortness of breath, chest tightness, or cough; ii) documented variable expiratory airflow limitation, which includes spirometry with a bronchodilator, of which an increase of FEV<sub>1</sub>>12% after administration of a bronchodilator is indicative of asthma [18,19].

Asthma exacerbation, as defined by the American Thoracic Society (ATS) and European Respiratory Society (ERS), is a worsening in symptoms and/or lung function, and/or increased rescue bronchodilator use, for at least two days. We classify it as a moderate

exacerbation if no hospital admission or emergency department visit is required, whereas an admission or emergency department visit, along with oral corticosteroid treatment for at least 3 days, denotes a severe exacerbation [20].

Lung function tests were done using easy-On-PC<sup>®</sup> device, and interpretations of FEV<sub>1</sub> readings, FEV<sub>1</sub>/FVC ratio, and other parameters were performed using the ATS Guideline and ERS Technical Statement [21]. These lung function tests were done on outpatient clinic follow-ups when patients were not in exacerbations and were on controller medications.

Patients in different groups were further studied and compared for their use of controller medications for the past year from their first documented exacerbation during the study period. This included the use of oral Monteleukast, ICS only, and long-acting  $\beta$  agonist with ICS (LABA+ICS). For this study in particular and to establish uniformity, we have chosen 2021 GINA guidelines [21].

Patients admitted with bronchiolitis, bronchopneumonia, and upper airway obstruction and previously diagnosed with cystic fibrosis, tuberculosis, chronic lung disease, congenital cardiac diseases, and immune deficiency syndrome were excluded from the study.

## Statistical analysis

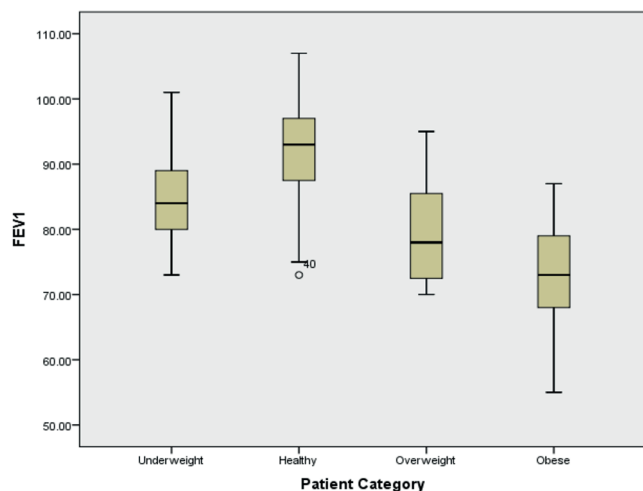
Data were analyzed using IBM SPSS Statistics for Windows, Version 22.0, released in 2013 (IBM, Armonk, NY, USA). Categorical variables were labeled as frequency and percentages, while continuous variables were conveyed as mean and standard deviation. Means were analyzed using the analysis of variance test and categorical data was analyzed using the Chi-square test, to assess for significant differences between the groups.  $p \leq 0.05$  was considered significant, with a type I error of 5%.

## Results

Our study included 90 asthma patients who met the eligibility criteria during the designated period. 21 (23.33%) patients were identified as underweight (less than the 5<sup>th</sup> percentile), 28 (31.11%) patients were classified as having a healthy weight (between the 5<sup>th</sup> and less than the 85<sup>th</sup> percentile), 23 (25.55%) patients were categorized as overweight (between the 85<sup>th</sup> and less than the 95<sup>th</sup> percentile), and 18 (20.0%) patients were obese (equal to or greater than the 95<sup>th</sup> percentile). Table 1 displays the demographic characteristics of asthmatic patients stratified by their BMI and the medications used for treatment. The age and gender distribution were comparable in all four groups. The mean duration of asthma diagnosis in years was comparable across all four groups and was unrelated to the BMI of the patients ( $p=0.16$ ). No significant association was found between the age of the patients and their BMI ( $p=0.14$ ). There were no significant differences between the groups as per serum immunoglobulin E levels and the number of patients with eczema, allergic rhinitis, and allergic conjunctivitis in the four groups.

There was a significant difference in the use of inhaled LABA+ICS across groups ( $p=0.01$ ), with the highest proportion of patients using this treatment in the obese group (83.33%). The use of Monteleukast was not significantly different across the groups ( $p=0.09$ ). There was a statistically significant difference in FEV<sub>1</sub> predicted (%) between the four groups ( $p<0.001$ ), with the obese group having the lowest FEV<sub>1</sub> predicted (72.94 $\pm$ 8.13), followed by the overweight group (79.56 $\pm$ 8.27), the underweight group (84.66 $\pm$ 6.08), and the healthy weight group, which had the highest FEV<sub>1</sub> predicted (91.46 $\pm$ 5.58) (Table 1 and Figure 1). The FEV<sub>1</sub>/FVC

ratio was also significantly lower in the obese group ( $70.55 \pm 15.99$ ) and the overweight group ( $74.69 \pm 12.63$ ) as compared to other groups ( $p < 0.001$ ). Mean asthma exacerbations per year were signif-



**Figure 1.** Comparison of forced expiratory volume in 1 second (FEV<sub>1</sub>) and body mass index categories.

icantly high ( $3.22 \pm 0.94$ ) in obese patients, followed by overweight participants ( $2.91 \pm 0.79$ ) and underweight ( $2.42 \pm 0.59$ ) participants ( $p < 0.01$ ). Conversely, participants with a healthy weight had the lowest number of exacerbations ( $1.92 \pm 0.71$ ). Additionally, the mean LOS per admission was significantly shorter for patients with a healthy weight ( $2.0 \pm 0.81$ ) as compared to those who were underweight ( $2.33 \pm 0.96$ ), overweight ( $2.91 \pm 0.99$ ), and obese ( $3.2 \pm 0.81$ ) ( $p < 0.001$ ). A higher proportion of underweight (85.71%), obese (83.33%), and overweight participants (73.91%) required HDU care compared to the healthy weight group (57.14%) ( $p < 0.001$ ). The average LOS at the HDU was also significantly longer in the underweight ( $1.9 \pm 0.74$ ), overweight ( $2.1 \pm 0.52$ ), and obese groups ( $2.4 \pm 0.91$ ) compared to the healthy weight group ( $1.65 \pm 0.67$ ), with  $p$  less than 0.001. These findings are presented in Table 2.

## Discussion

This study aimed to examine the association between BMI and asthma exacerbations in pediatric patients. The results revealed a statistically significant difference in mean asthma exacerbations per year ( $p < 0.01$ ) between the four groups, with the highest mean exacerbation rate in the obese category ( $3.22 \pm 0.94$ ), followed by underweight patients ( $2.42 \pm 0.59$ ), and the lowest number of exacerbations in the healthy weight category ( $1.92 \pm 0.71$ ). We obtained findings

**Table 1.** Demographic and clinical characteristics (n=90).

	Underweight group	Healthy weight group	Overweight group	Obese group	p
Patient, n	21	28	23	18	
Age (years)	$10.34 \pm 2.80$	$12.29 \pm 3.27$	$11.59 \pm 2.94$	$11.32 \pm 1.91$	0.14
Male:female	1.5:1	1.3:1	1.6:1	1.4:1	
Weight (kg)	$20.54 \pm 1.52$	$41.31 \pm 1.39$	$54.12 \pm 1.75$	$67.29 \pm 1.28$	0.00
Height (cm)	$125.89 \pm 1.97$	$150.3 \pm 2.14$	$156.53 \pm 1.76$	$161.18 \pm 1.54$	0.00
Average duration on diagnosis with asthma (years)	$4.48 \pm 1.23$	$6.7 \pm 1.64$	$5.9 \pm 1.42$	$6.3 \pm 1.29$	0.16
Serum immunoglobulin E	$348 \pm 80.87$	$375 \pm 103.43$	$360 \pm 96.16$	$393 \pm 110.30$	0.10
Eczema, n (%)	5 (23.80)	6 (28.57)	5 (21.73)	4 (22.22)	0.12
Allergic rhinitis, n (%)	7 (33.33)	6 (28.57)	8 (34.78)	6 (33.33)	0.19
Allergic conjunctivitis n (%)	2 (9.52)	2 (7.14)	3 (13.04)	2 (11.11)	0.09
Use of inhaled LABA with ICS, n (%)	11 (52.38)	16 (57.14)	14 (60.86)	15 (83.33)	0.01
Use of ICS only, n (%)	8 (38.09)	11 (39.28)	9 (39.13)	3 (16.66)	0.04
Use of Montelukast, n (%)	15 (71.4)	22 (78.6)	17 (73.9)	14 (77.7)	0.09

LABA, long acting  $\beta$ -agonist; ICS, inhaled corticosteroids.

**Table 2.** Outcome variables and comparison of patients in the four groups.

	Underweight group	Healthy weight group	Overweight group	Obese group	p
Patient, n	21	28	23	18	
FEV <sub>1</sub> predicted (%)	$84.66 \pm 6.08$	$91.46 \pm 8.58$	$79.56 \pm 8.27$	$72.94 \pm 8.13$	<0.001
FEV <sub>1</sub> /FVC (%)	$83.47 \pm 10.07$	$85.75 \pm 9.23$	$74.69 \pm 12.63$	$70.55 \pm 15.99$	<0.001
Mean asthma exacerbation per year	$2.42 \pm 0.59$	$1.92 \pm 0.71$	$2.91 \pm 0.79$	$3.22 \pm 0.94$	<0.01
Average LOS per admission	$2.33 \pm 0.96$	$2.0 \pm 0.81$	$2.91 \pm 0.99$	$3.2 \pm 0.81$	<0.001
Number of patients needing HDU care, n (%)	18 (85.71)	16 (57.14)	17 (73.91)	15 (83.33)	<0.001
Average LOS at HDU	$1.9 \pm 0.74$	$1.65 \pm 0.67$	$2.1 \pm 0.52$	$2.4 \pm 0.91$	<0.001

FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; LOS, length of stay; HDU, high dependency unit.

that were consistent with prior research that showed those who are both obese and asthmatic experience more symptoms, as well as more frequent and severe exacerbations, increasing the burden of the disease [22-24]. Moreover, our findings of an increased number of exacerbations in both obese and underweight patients align with previous research that indicated a link between extreme weights and increased asthma exacerbations [11,12,25]. Lang *et al.* highlight similar findings, with obese asthmatic children making up 26.2% of the cohort with a greater likelihood of having severe disease [odds ratio (OR) 1.40, 95% confidence interval (CI) 1.06-1.85]. Moreover, through this study, it is seen that both underweight and obese children have worse lung function in comparison to children with a normal weight [7]. The connection between low body weight and asthma has not been thoroughly established, and earlier research has suggested that men with lower body weight are at a greater risk of developing asthma. Several other studies done previously showed that extremes of weight are associated with increased asthma exacerbation and poorer outcomes [11,12,25]. Two large cross-sectional studies conducted in Israel and Italy found an association between being underweight and the prevalence of asthma [25,26]. In the Italian study, underweight men had a significantly higher age-adjusted prevalence of self-reported asthma compared to men of normal weight. The OR for men with a BMI less than 20 kg/m<sup>2</sup> was 1.4, and the 95% CI was 1.2-1.8 [23].

The predicted FEV<sub>1</sub> showed a significant difference between the groups. Moreover, the predicted FEV<sub>1</sub> was seen to be the lowest among obese patients (72.94±8.13) and highest in patients of healthy weight (91.468.58). Obese patients also had the lowest FEV<sub>1</sub>/FVC (70.55±15.99) when compared to the other three groups (p<0.001), with patients of healthy weight having the highest FEV<sub>1</sub>/FVC (85.75±9.23). Another study demonstrated that obese children were more likely to have increased β agonists used (OR 1.17, 95% CI 1.06-1.29) in comparison to normal-weight children, thus highlighting that childhood obesity is associated with worse asthma control [3]. In addition, a previous meta-analysis conducted showed similar results and revealed that childhood obesity is linked to having a lower FEV<sub>1</sub>/FVC ratio [27]. Furthermore, spirometry findings were found to be significantly decreased in the underweight group as well, with a predicted FEV<sub>1</sub>/FVC of 83.47±10.07. Davidson *et al.* report similar findings, in which underweight participants demonstrated lower FVC and vital capacity compared to normal-weight participants [28]. This finding may be attributed to nutritional deficiencies that may be present in children with a lower BMI, including vitamin D deficiency, which has been reported to increase the annual number of asthma exacerbations [29].

The average LOS per admission was also significantly impacted (p<0.001) with obese patients having a prolonged LOS per admission (3.20.81) compared to the other three categories. Furthermore, the number of patients needing HDU care, and their average LOS were also statistically significant (p<0.001) between the four groups. Furthermore, a previous study found that obese children had significantly longer hospital lengths of stay (9.8±7.0 versus 6.5±3.4 days, p<0.1) [24]. This can also be inferred from our study, where obese children have a significantly longer hospital stay (3.20.81, p<0.001). Our results were in line with a previous study that showed obese asthmatics have ≥3 days of hospital stay when compared to non-obese patients [30].

The mean asthma exacerbation per year was seen to be significant (p<0.001) among the four groups, with patients of healthy weight having the fewest admissions (1.920.71). A study conducted on the North European asthmatic pediatric population also found that there is an increased risk of asthma exacerbation in obese patients as compared to non-obese patients (OR 1.17, 95% CI 1.03-

1.34; I<sup>2</sup>: 54.7%) [23]. Kattan *et al.* found that higher BMI was associated with more exacerbations (R=0.18, p=0.06) among female pediatric patients, primarily [31].

In the current study, there was a significant difference in the use of inhaled LABA+ICS among the four groups (p=0.01). Another study reported increased use of LABA+ICS (OR 1.37, 95% CI 1.05-1.78) as compared to the non-obese group [32]. One more study observed that an increase in the use of ICS was associated with a rise in BMI per year, and individuals who frequently visited the emergency department had a higher BMI [33].

While this study does not explore the impact that weight loss can have on asthma, there have been studies that assess the benefits of weight loss on asthma. Silva *et al.* conducted a study where adolescents underwent a 1-year weight loss interdisciplinary intervention, resulting in an improvement in both lung function and pro/anti-inflammatory adipokines. There was an increase in adiponectin and a decrease in CRP and leptin levels. Moreover, there was a decrease in asthma severity [34]. Other studies have demonstrated that a reduction in BMI can improve asthma control, asthma-related quality of life, lung function indices, and fewer acute asthma attacks [35,36]. Similarly, another study reported that weight loss in obese patients significantly improved respiratory parameters, including FEV<sub>1</sub> and FVC [37].

This study's limitations include the absence of a control group without asthma to compare asthmatic BMI patients. Moreover, the potential confounding factors that may influence asthma outcomes, like parental education level, gastroesophageal reflux disease diagnosis, and diabetes mellitus diagnosis, were not adjusted [3]. The asthmatic patients were not classified based on severity. Finally, this study could not discern whether the raised BMI was due to the ICS given for the control of severe asthma, which could account for the increased number of asthma exacerbations. A previous study found that the increased use of ICS leads to an increased trend in BMI per year [33].

## Conclusions

In conclusion, this study highlights the association between increasing BMI and asthma exacerbations in pediatric patients. Obese patients with asthma had more frequent exacerbations, poorer lung function, and longer hospital stays compared to patients of healthy weight. Identifying and addressing the impact of obesity on asthma management is essential to improving outcomes for pediatric patients with asthma. Further prospective research is needed to determine effective interventions to manage asthma in obese pediatric patients.

## References

1. Everaere L, Ait Yahia S, Bouté M, et al. Innate lymphoid cells at the interface between obesity and asthma. *Immunology* 2018;153:21-30.
2. Alhekail GA, Althubaiti A, AlQueflie S. The association between body mass index and frequency of emergency department visits and hospitalization for asthma exacerbation in a pediatric population. *Ann Saudi Med* 2017;37:415-9.
3. Quinto KB, Zuraw BL, Poon KYT, et al. The association of obesity and asthma severity and control in children. *J Allergy Clin Immunol* 2011;128:964-9.
4. Shan LS, Zhou QL, Shang YX. Bidirectional association between asthma and obesity during childhood and adoles-

- cence: a systematic review and meta-analysis. *Front Pediatr* 2020;8:576858.
5. Kim SH, Sutherland ER, Gelfand EW. Is there a link between obesity and asthma?. *Allergy Asthma Immunol Res* 2014;6: 189-95.
  6. Reyes-Angel J, Kaviany P, Rastogi D, Forno E. Obesity-related asthma in children and adolescents. *Lancet Child Adolesc Health* 2022;6:713-24.
  7. Lang JE, Hossain J, Smith K, Lima JJ. Asthma severity, exacerbation risk, and controller treatment burden in underweight and obese children. *J Asthma* 2012;49:456-63.
  8. Holguin F, Bleecker ER, Busse WW, et al. Obesity and asthma: an association modified by age of asthma onset. *J Allergy Clin Immunol* 2011;127:1486-93.e2.
  9. Santamaria F, Montella S, Greco L, et al. Obesity duration is associated to pulmonary function impairment in obese subjects. *Obesity* 2011;19:1623-8.
  10. Forno E, Lescher R, Strunk R, et al. Decreased response to inhaled steroids in overweight and obese asthmatic children. *J Allergy Clin Immunol* 2011;127:741-9.
  11. Kang M, Sohn SJ, Shin MH. Association between body mass index and prevalence of asthma in Korean adults. *Chonnam Med J* 2020;56:62-7.
  12. Luder E, Ehrlich RI, Lou WYW, et al. Body mass index and the risk of asthma in adults. *Respir Med* 2004;98:29-37.
  13. Shore SA. Obesity and asthma: possible mechanisms. *J Allergy Clin Immunol* 2008;121:1087-93.
  14. Huang YJ, Chu YC, Chen CW, et al. Relationship among genetic variants, obesity traits and asthma in the Taiwan Biobank. *BMJ Open Respir Res* 2022;9:e001355.
  15. Han X, Zhu Z, Xiao Q, et al. Obesity-related biomarkers underlie a shared genetic architecture between childhood body mass index and childhood asthma. *Commun Biol* 2022;5:1098.
  16. Cole TJ, Faith MS, Pietrobelli A, Heo M. What is the best measure of adiposity change in growing children: BMI, BMI %, BMI z-score or BMI centile?. *Eur J Clin Nutr* 2005;59:419-25.
  17. National Center for Health Statistics. Vital and health statistics. Evaluation of alternative body mass index (BMI) metrics to monitor weight status in children and adolescents with extremely high BMI using CDC BMI-for-age growth charts. 2022. Available from: [https://www.cdc.gov/nchs/data/series/sr\\_02/sr02-197.pdf](https://www.cdc.gov/nchs/data/series/sr_02/sr02-197.pdf).
  18. Global Initiative for Asthma. 2022 GINA Main Report. Available from: <https://ginasthma.org/gina-reports/>. Accessed: 27/05/2023.
  19. Rothe T, Spagnolo P, Bridevaux PO, et al. Diagnosis and management of asthma - The Swiss guidelines. *Respiration* 2018; 95:364-80.
  20. Forno E, Celedón JC. Predicting asthma exacerbations in children. *Curr Opin Pulm Med* 2012;18:63-9.
  21. Graham BL, Steenbruggen I, Barjaktarevic IZ, et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. *Am J Respir Crit Care Med* 2019;200: e70-88.
  22. Peters U, Dixon AE, Forno E. Obesity and asthma. *J Allergy Clin Immunol* 2018;141:1169-79.
  23. Ahmadizar F, Vijverberg SJH, Arets HGM, et al. Childhood obesity in relation to poor asthma control and exacerbation: a meta-analysis. *Eur Respir J* 2016;48:1063-73.
  24. Okubo Y, Nochioka K, Hataya H, et al. Burden of obesity on pediatric inpatients with acute asthma exacerbation in the United States. *J Allergy Clin Immunol Pract* 2016;4:1227-31.
  25. Negri E, Pagano R, Decarli A, La Vecchia C. Body weight and the prevalence of chronic diseases. *J Epidemiol Community Health* 1988;42:24-9.
  26. Lusky A, Barell V, Lubin F, et al. Relationship between morbidity and extreme values of body mass index in adolescents. *Int J Epidemiol* 1996;25:829-34.
  27. Forno E, Han YY, Mullen J, Celedón JC. Overweight, obesity, and lung function in children and adults-a meta-analysis. *J Allergy Clin Immunol Pract* 2018;6:570-81.e10.
  28. Davidson WJ, Mackenzie-Rife KA, Witmans MB, et al. Obesity negatively impacts lung function in children and adolescents. *Pediatr Pulmonol* 2014;49:1003-10.
  29. Aziz DA, Abbas A, Viquar W, Hussain AM. Association of vitamin D levels and asthma exacerbations in children and adolescents: experience from a tertiary care center. *Monaldi Arch Chest Dis* 2022;93:2230.
  30. Luthe SK, Hirayama A, Goto T, et al. Association between obesity and acute severity among patients hospitalized for asthma exacerbation. *J Allergy Clin Immunol Pract* 2018;6: 1936-41.e4.
  31. Kattan M, Kumar R, Bloomberg GR, et al. Asthma control, adiposity, and adipokines among inner-city adolescents. *J Allergy Clin Immunol* 2010;125:584-92.
  32. McGarry ME, Castellanos E, Thakur N, et al. Obesity and bronchodilator response in black and Hispanic children and adolescents with asthma. *Chest* 2015;147:1591-8.
  33. Han J, Nguyen J, Kim Y, et al. Effect of inhaled corticosteroid use on weight (BMI) in pediatric patients with moderate-severe asthma. *J Asthma* 2019;56:263-9.
  34. Da Silva PL, De Mello MT, Cheik NC, et al. Interdisciplinary therapy improves biomarkers profile and lung function in asthmatic obese adolescents. *Pediatr Pulmonol* 2012;47:8-17.
  35. Willeboordse M, Van De Kant KDG, Tan FES, et al. A multifactorial weight reduction programme for children with overweight and asthma: a randomized controlled trial. *PLoS One* 2016;11:e0157158.
  36. Luna-Pech JA, Torres-Mendoza BM, Luna-Pech JA, et al. Normocaloric diet improves asthma-related quality of life in obese pubertal adolescents. *Int Arch Allergy Immunol* 2014;163:252-8.
  37. Stenius-Aarniala B, Poussa T, Kvarnström J, et al. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ* 2000;320:827-32.