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

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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 in pediatric asthmatic patients. This retrospective study was conducted at the Aga Khan University Hospital from 2019 to 2022. Children and adolescents with asthma exacerbation 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 FEV_1 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_1 (91.46±8.58) and FEV_1/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_1 and FEV_1/FVC, increased length of stay at admission, and increased stay in the HDU.

Key words: Body mass index (BMI), asthma exacerbation, lung volumes, obesity

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 making 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 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, duration of obesity [9], presence of significant co-morbids, 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 length of stay 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 exacerbation in children and adolescents with asthma.

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 FEV_1 and FEV_1/FVC ratio, number of asthma exacerbations, mean LOS per admission, HDU admission and length of stay at High Dependency Unit (also known as Special Care Unit, is a level below the Intensive Care Unit). Patients were categorized into four groups: i) Underweight with BMI less than the 5th percentile, ii) Healthy-weight with BMI between 5th percentile to less than the 85th percentile, iii) Overweight with BMI between 85th percentile to less than the 95th percentile and iv) Obese with BMI 95th percentile or greater. The WHO guidelines were used to categorize patients as per BMI. BMI is defined as body mass in kilogram (kg) divided by the square of the body height in meters (m^2), and is expressed in units of kg/m^2 [16]. These values were then

plotted on BMI centile charts published by Centers for Disease Control and Prevention (CDC), to categorize the patients in four different groups [17].

Diagnosis of asthma was according to the Global Initiative for Asthma (GINA) guidelines: i) identifying characteristic episodic respiratory symptoms including wheezing, shortness of breath, chest tightness or cough, and ii) documented variable expiratory airflow limitation, which includes spirometry with bronchodilator, of which an increase of FEV_1 >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 moderate exacerbation if no hospital admission or emergency department (ED) visit is required, whereas an admission or ED visit, along with oral corticosteroid treatment for at least three days, denotes a severe exacerbation [20].

Lung function tests were done using easy-On-PC® device, and interpretations of FEV_1 readings, FEV_1/FVC ratio and other parameters were performed using ATS Guideline and ERS Technical Statement [21]. These lung function tests were done on outpatient clinic follow-up 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 use of oral Monteleukast, inhaled corticosteroids (ICS) only and long acting beta agonist with inhaled corticosteroids (LABA+ICS). For this study in particular and to establish uniformity, we have chosen 2021 GINA guidelines [21].

Patients admitted with bronchiolitis, bronchopneumonia, 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 Corp. released 2013, IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Categorical variables were labeled as frequency and percentages, while continuous variables were conveyed as mean and standard deviation. Means were analyzed using the ANOVA test and categorical data was analyzed using Chi-square test, to assess for significant differences between the groups. A p-value of ≤0.05 was considered significant, with a type I error of 5%.

Results

A total of 90 patients with asthma who met the eligibility criteria were included in our study during the designated period. Twenty-one (23.33%) patients were identified as underweight (less than the 5th percentile), 28 (31.11%) patients were classified as having a healthy weight (between the 5th and less than the 85th percentile), 23 (25.55%) patients were categorized as overweight (between the 85th and less than the 95th percentile), and 18 (20.0%) patients were obese (equal to or greater than the 95th percentile). Table 1 presents the demographic characteristics of the asthmatic patients stratified by their BMI and the medications used for their 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 (IgE) levels and number of patients with eczema, allergic rhinitis and allergic conjunctivitis in four groups. There was a significant difference in the use of inhaled LABA with inhaled steroids (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_1 predicted (%) between the four groups (p<0.001), with the obese group having the lowest FEV_1 predicted (72.94±8.13), followed by the overweight group (79.56±8.27), the underweight group (84.66±6.08) and the healthy weight group, which had the highest FEV1 predicted (91.46±5.58) (Table 1 and Figure 1). The FEV1/FVC ratio was also significantly lower in the obese group (70.55±15.99) and the overweight group (74.69±12.63) as compared to other groups (p<0.001). Mean asthma exacerbations per year were significantly high (3.22±0.94) in obese patients, followed by overweight participants (2.91±0.79) and underweight (2.42±0.59) participants (p<0.01). Conversely, participants with a healthy weight had the lowest number of exacerbations (1.92±0.71). Additionally, the mean LOS per admission was significantly shorter for patients with a healthy weight (2.0±0.81) as compared to those who were underweight (2.33±0.96), overweight (2.91±0.99), and obese (3.2±0.81) (p<0.001). A higher proportion of underweight (85.71%), obese (83.33%) and overweight participants (73.91%) required High Dependency Unit (HDU) care compared to the healthy weight group (57.14%) (p <0.001). The average length of stay at the HDU was also significantly longer in the underweight (1.9±0.74), overweight (2.1±0.52) and the obese group (2.4±0.91) compared to the healthy weight group (1.65±0.67), with a p-value of 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 exacerbation per year (p<0.01) between the four groups, with the highest mean exacerbation rate in the obese category (3.22±0.94) followed by underweight patients (2.42±0.59) and the lowest number of exacerbations in the healthy weight category (1.92±0.71). We obtained findings 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 to have 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 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 odds ratio for men with a BMI less than 20 kg/m^2 was 1.4, and the 95% confidence interval was 1.2-1.8 [23].

The predicted FEV_1 showed a significant difference between the groups. Moreover, the predicted FEV_1 was seen to be the lowest among the obese patients (72.94±8.13) and highest in patients of healthy weight (91.46±8.58). Obese patients also had the lowest FEV_1/FVC (70.55±15.99) when compared to the other three groups (p<0.001) with patients of healthy weight having the highest FEV_1/FVC (85.75±9.23). Another study demonstrated that obese children were more likely to have increased B-agonists used (OR 1.17, 95% CI 1.06-1.29) as 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_1/FVC ratio [27]. Furthermore, spirometry findings were found to be significantly decreased in the underweight

group as well, with a predicted FEV_1/FVC of 83.47±10.07. Davidson *et al*. report similar findings, in which underweight participants have shown lower forced vital capacity and vital capacity compared to normal-weight participants [28]. This finding may be attributed to nutritional deficiencies that may be present in children with lower BMI, including vitamin D deficiency, which has been reported to increase the annual number of asthma exacerbations [29].

The average length of stay per admission was also significantly impacted (p<0.001) with obese patients having a prolonged length of stay per admission (3.2±0.81) compared to the other three categories. Furthermore, the number of patients needing HDU care and their average length of stay 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 *vs* 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 (3.2±0.81, 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 least admissions (1.92±0.71). 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 (OR 1.17, 95% CI 1.03-1.34; I^2: 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 with inhaled corticosteroids among the four groups (p=0.01). Another study reported increased use of LABA with inhaled corticosteroids (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 inhaled corticosteroids 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 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_1 and FVC [37].

The limitations of this study include the absence of a control group without asthma to compare the 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 inhaled corticosteroids 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 inhaled corticosteroids 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 improve outcomes in pediatric patients with asthma. Further prospective research is needed to determine effective interventions to manage asthma in obese pediatric patients.

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

	Underweight group	Healthy weight group	Overweight group	Obese group	p-value
Patient, n	21	28	23	18	
Age (Years)	10.34±2.80	12.29±3.27	11.59±2.94	11.32±1.91	0.14
Male : Female	1.5: 1	1.3:1	1.6: 1	1.4:1	
Weight (Kg)	20.54±1.52	41.31±1.39	54.12±1.75	67.29±1.28	0.00
Height (cm)	125.89±1.97	150.3±2.14	156.53±1.76	161.18±1.54	0.00
Average duration on diagnosis with asthma (Years)	4.48±1.23	6.7±1.64	5.9±1.42	6.3±1.29	0.16
Serum Immunoglobulin E (IgE)	348±80.87	375±103.43	360±96.16	393±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 (LABA+ICS) n (%)	11(52.38%)	16 (57.14%)	14(60.86%)	15 (83.3.3%)	0.01
Use of ICS only	8 (38.09%)	11(39.28%)	9(39.13%)	3(16.66%)	0.04
Use of Monteleukast 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-value
Patient, n	21	28	23	18	
FEV$_1$ Predicted (%)	84.66±6.08	91.46±8.58	79.56±8.27	72.94±8.13	<0.001
FEV$_1$/FVC (%)	83.47±10.07	85.75±9.23	74.69±12.63	70.55±15.99	<0.001
Mean Asthma Exacerbation per year	2.42±0.59	1.92±0.71	2.91±0.79	3.22±0.94	<0.01
Average LOS per admission	2.33±0.96	2.0±0.81	2.91±0.99	3.2±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 length of stay at HDU	1.9±0.74	1.65±0.67	2.1±0.52	2.4±0.91	<0.001

FEV$_1$=forced expiratory volume in 1 sec, FVC= forced vital capacity, HDU=High Dependency Unit
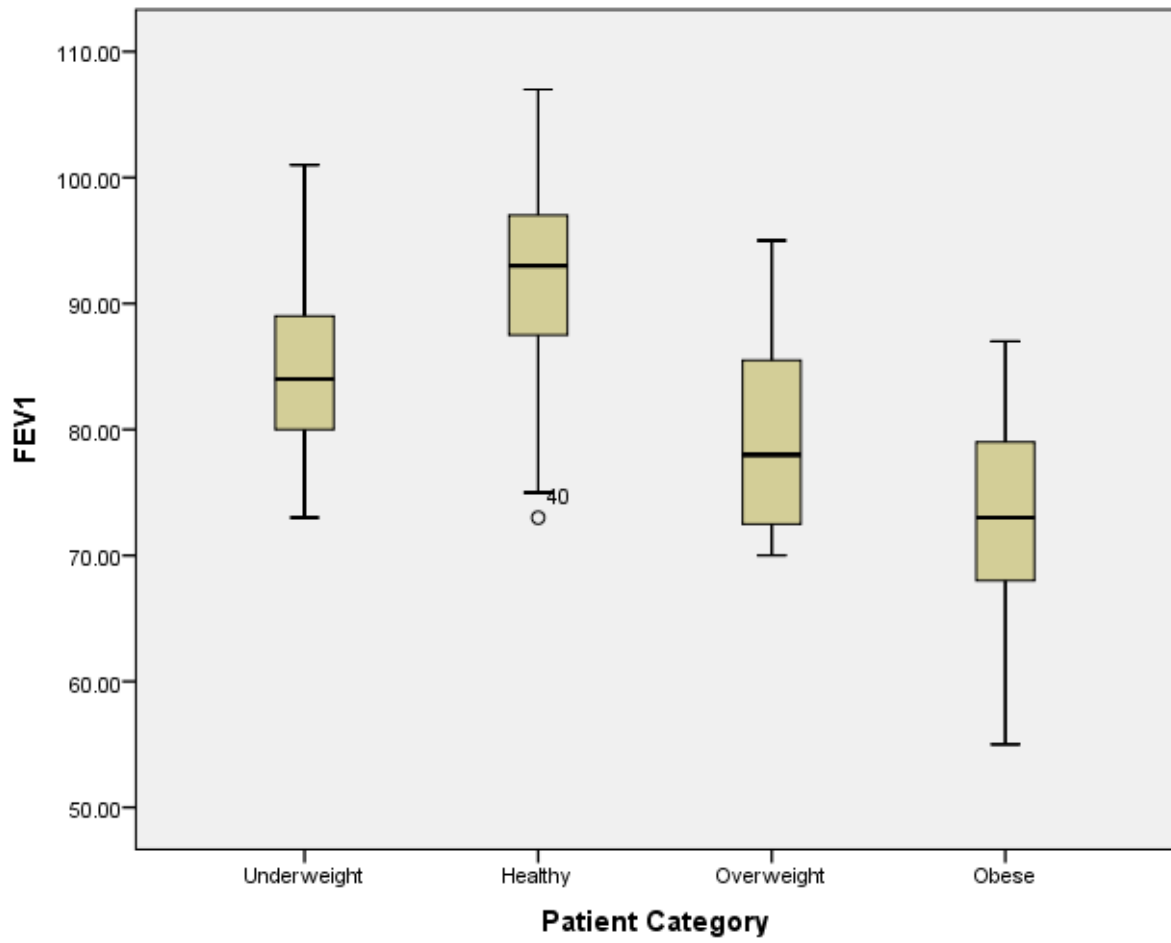
Figure 1. Comparison of forced expiratory volume in 1 second (FEV1) and body mass index (BMI) categories.