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Impact of Obesity on Childhood Asthma in Ismailia

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Abstract

Background: **Nowadays, asthma and obesity are two major chronic illnesses in children and adolescents. Obesity is an important risk factor for asthma and a significant disease modifier. Obesity is associated with low-grade systemic inflammation, which can interact with asthma inflammatory cascades, both in terms of inducing and worsening asthma.** ***Aim:*** **To assess the impact of obesity on asthma in children.** ***Subjects and methods:*** **A descriptive cross-sectional study was conducted among obese and non-obese asthmatic children in the age group from 3 years to 12 years old, attending the pediatric clinic of Suez Canal University Hospital in Ismailia, Egypt. Data was collected from the study population using a pre-designed questionnaire including a full history of asthma.** ***Results:*** **The study showed that obese patients had a significantly higher association with frequency of uncontrolled asthma. Likewise, acute attacks of severe type were significantly higher among obese patients. Meanwhile, obese patients were found to have a higher significant frequency of ICU admission and hospitalization. Moreover, obese patients have increased odds of having a severe form of asthma by 18.066 times (OR= 18.06, p=0.045).** ***Conclusions:*** **Obesity among asthmatic children is linked with more severe asthma exacerbations and uncontrolled asthma.**

Keywords: Uncontrolled Asthma, children, Adolescents

Introduction

Nowadays, asthma and obesity are two major chronic illnesses in children and adolescents. Asthma is a worldwide health issue that influences more than 300 million people of all ages and ethnic groups[1]. The International Study of Asthma and Allergies in Childhood, an international multicenter epidemiological study, stated that the prevalence of asthma is increasing slightly globally[2] and different risk factors such as bad dietary habits, exposure to tobacco smoke, and pollution are probable causes that are associated with changing the epidemiology of asthma[3]. The prevalence of overweight and obesity in children increased by 47.1% worldwide between 1980 and 2013, mainly because of unhealthy dietary habits and choices, a decrease in physical exercise, and an increase in sedentary lifestyles [4]. The parallel increase in the prevalence of childhood obesity in the last decade has raised concerns about a possible correlation between asthma and obesity as obesity is considered a significant risk factor for asthma as well as a major disease modifier[5]. Different studies have shown that being overweight or obese is associated with an increased risk of developing bronchial asthma[6,7]. The possible mechanisms of

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how obesity can lead to asthma include increased weight on the chest wall causing breathing at lower lung volumes [8] and/or the pro-inflammatory mediator released by the adipocytes[9]. These mechanisms may also cause obese children with asthma to experience severe asthma and more symptoms than non-obese asthmatic children[10]. A growing amount of evidence shows that obesity is associated with low-grade systemic inflammation "meta-inflammation"[11], which interacts within asthma inflammatory cascades, regardless of its endotype or severity, both in terms of inducing and worsening asthma[12]. Meanwhile, when considering the correlation between asthma and obesity at a molecular level, the following four cytokines IL-4, IL-5, IL-13, and IL-33 have a prominent pro-inflammatory role in T2-high asthma and contribute to maintaining the lean state, while the reduced IL-33 levels are associated with increased body mass index [13]. Also, IL-4 and IL-13 induce the expression of two anti-inflammatory cytokines TGF-β and IL-10 by M2 macrophages[14]. Obese children with asthma may respond less to prophylactic controller medications such as inhaled corticosteroids[15]. Moreover, they are more likely to be given oral corticosteroid courses than non-obese asthmatic patients and have a decreased response to these courses[16]. The interplay between asthma and obesity is a complex process and has not yet been completely explained, so this study aims to assess the impact of obesity on asthma in children attending the pediatric clinic in Suez Canal University Hospital.

Subjects and Methods

A descriptive cross-sectional study was conducted among 84 asthmatic children attending the pediatric clinic in Suez Canal University Hospital in Ismailia, Egypt. We enrolled both obese and non-obese asthmatic children with age groups from 3 years to 12 years old. Diagnosis of asthma is based on a compatible history of recurrent episodes of wheezing, cough, difficulty breathing, and chest tightness, a physical exam confirming airway obstruction (e.g., wheezing) that improves with short-acting beta agonist (SABA), and absence of an alternative explanation according to the global initiative for asthma guidelines in 2017[17]. The obese child is a child with a body mass index >95th percentile for age and sex[18] using the Egyptian growth charts for children[19]. We excluded any patient with other metabolic disorders, chronic respiratory diseases, immunodeficiency disorders, or respiratory infections. Ethical approval from the research ethics committee of the faculty of medicine, at Suez Canal University was obtained.

Data Collection

We collected data from study participants using a pre-designed questionnaire including a full medical history including history of hospitalization, PICU admission, and medication history obtained from the caregivers of the asthmatic patients after their approval for participating in the study through written informed consent. We assessed asthma control and risk factors for asthma attacks according to the global initiative for asthma guidelines in 2017[17] using the following questionnaire: 1) Daytime asthma symptoms more than twice/ week?) 2) Any night symptoms due to asthma? 3) Reliever needed for symptoms more than twice/week? 4) Any activity limitation due to asthma? 5) FEV1 or peak flow < 80%?

Interpretation

Yes:1 point, no :0 points, and the total score was classified as the following: 0 points =well-controlled asthma symptoms.

1–2 points =partly controlled asthma symptoms. ≥3 points =uncontrolled asthma symptoms. Meticulous clinical examination data included chest examination, assessment of weight /height, and the calculated body mass index. Laboratory investigations: CBC and total IgE. Spirometry in children aged ≥6 years was used to assess the asthmatic patient as follows: forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) < 80% with a 12% improvement in FEV1 after SABA is specific for the diagnosis of asthma[17]. Imaging techniques: chest x-ray.

Statistical Analysis

The data was collected, coded, and entered into the computer *via* the Excel 2013 program. SPSS program version 20 was used for data analysis. Data was analyzed and presented as numbers and percentages using tables, and graphs with the CI at 95%. p-value of 0.05 was used as the limit of statistical significance. T-test and chi-square tests were used as appropriate.

Results

Table (1) summarizes the baseline characteristics of the studied sample. Obese asthmatic patients comprised 64.3% of the total patients, while non-obese asthmatic patients comprised 35.7 %. The obese asthmatic patients had significantly lower ages than non-obese patients (6.48 ± 2.48 *vs* 9.93 ± 1.82) (p<0.001).

Table 1. Clinical characteristics of the study population

Clinical characteristics	Total (n=84)	Obese group (n=54)	Non-obese group (n=30)		Test value	p-value
Age (years)						
mean ± SD	7.71 ± 2.80	6.48 ± 2.48	9.93 ± 1.82		231	**<0.001** [a]
median (range)	8(3–12)	6(3–12)	10.5	(6 – 12)		
Gender, n (%)						
Male	42 (50)	31 (57.4)	11	(36.7)	3.32	0.7 [b]
Female	42 (50)	23 (42.6)	19	(63.3)		
Residency, n (%)						
Urban	43 (51.2)	27 (50)	16	(53.3)	0.09	0.8 [b]
Rural	41 (48.8)	27 (50)	14	(46.7)		
Family Smoking, n (%)						
Positive	44 (52.4)	28 (51.9)	16	(53.3)	0.02	0.9 [b]
Negative	40 (47.6)	26 (48.1)	14	(46.7)		
Family History of Allergies						
Positive	40 (47.6)	27 (50)	13	(43.3)	0.34	0.62 [b]
Negative	44 (42.4)	27 (50)	17	(56.7)		

[a]= *Mann Whitney U test.* [b]= *Chi-square test. Statistical significance at P < 0.05*

About half of the total asthmatic patients had a positive family smoking history (52.4%) and a positive family history of allergies (47.6%). Table (2) shows the anthropometric measurements of the studied asthmatic patients. The mean weight of the obese group was 40.67 ± 9.04 kg, while the mean height was 1.17 ± 0.16 m, and the mean BMI was 29.12 ± 3.02 kg/m^2. On the other hand, the mean weight of the non-obese group was 33.47 ± 9.66 kg, while the mean height was 1.39 ± 0.12 m and the mean BMI was 20.60 ± 1.68 kg/m^2. Table (3) shows that obese patients had a

significantly higher association with the frequency of uncontrolled asthma (p<0.001). Likewise, acute attacks of severe type were significantly higher among obese patients compared to non-obese patients (p<0.001). Meanwhile, obese patients were found to have a higher frequency of ICU admission (p=0.006) and hospitalization (p<0.001) compared to non-obese patients. Figures (1) and (2) show that the studied obese asthmatic patients had significantly lower spirometry parameters (FEV1, FVC, and PEF) and higher Ig E levels compared to non-obese patients. Moreover, obese asthmatic patients had significantly lower hemoglobin levels compared to non-obese asthmatic patients (8.75 ± 1.67 vs 11.08 ± 2.36) (p<0.001) and had significantly higher CRP levels compared to non-obese asthmatic patients (7.89 ± 3.27 vs 4.67 ± 2.38) (p<0.001). In Table (4) logistic regression analysis was used to assess predictors of asthma severity among asthmatic pediatric patients. It was found that increased severity of asthma was associated with higher serum Ig E (OR= 1.040, p=0.001) and obesity (OR= 18.06, p=0.045). Moreover, obese patients had increased odds of having a severe form of asthma compared to non-obese patients by 18.066 times. Table (5) shows the multivariable linear regression analysis used to assess predictors of hospitalization frequency among asthmatic pediatric patients. R2 =0.411, where 41.1 % of the variability among asthmatic pediatric patients can be explained by this linear model. Increased risk of hospitalizations among patients was associated with increased age (β= 0.150, p=0.045), higher serum Ig E (β= 0.010, p<0.001), and obesity (β= 1.56, p=0.001), where there is an increase in the odds of hospitalization frequency by 1.56 times in obese asthmatic patients compared to non-obese ones.

Discussion

Asthma and obesity are two major health problems affecting many people worldwide. In the present study, obese asthmatic children represent 64.3% of the total asthmatic patients and have significantly lower ages than non-obese patients (6.48 ± 2.48 vs 9.93 ± 1.82) (p<0.001).

Table 2: Anthropometric measurements of the studied sample

Clinical characteristics	Total (n=84)	Obese group (n=54)	Non-obese group (n=30)	Test value	p-value
Weight (Kg)					
mean ± SD	36.04 ± 10.1	40.67 ± 9.04	33.47 ± 9.66	460	**0.001** [a]
median (range)	34.9 (20.2 – 57.1)	41.45 (23 - 55.1)	32.6 (20.2 – 57.1)		
Height (m)					
mean ± SD	1.25 ± 0.18	1.17 ± 0.16	1.39 ± 0.12	241	**<0.001** [a]
median (range)	1.26 (0.94 – 1.5)	1.14 (0.94 – 1.5)	1.4 (1.14 – 1.53)		
BMI (kg/m²)					
mean ± SD	22.86 ± 2.68	29.12 ± 3.02	20.60 ± 1.68	165.5	**<0.001** [a]
median (range)	23 (17.6 – 31.5)	29.77 (27.9 – 31.5)	20.2 (17.6 – 23.6)		

[a]= *Mann Whitney U test. Statistical significance at P < 0.05*

Age forms one of the most important confounders that affect the relationship between asthma and obesity. Chen et al.[20], in their large prospective study, reported that early childhood asthma contributed to the development of obesity during later childhood and adolescence compared to non-asthmatic controls.

Table 3. Comparison of different clinical characteristics between the two groups					
Clinical characteristics	**Total (n=84)**	**Obese (n=54)**	**Non-obese (n=30)**	**Test value**	**p-value**
Asthma control					
Controlled	18 (21.4)	6 (11.1)	12 (40)		
Partially controlled	34 (40.5)	17 (31.5)	17 (56.7)	25.3	**<0.001** [a]
Uncontrolled	32 (38.1)	31 (57.4)	1 (3.3)		
The severity of acute attacks					
Mild	22 (26.2)	10 (18.5)	12 (40)		
Moderate	30 (35.7)	13 (24.1)	17 (56.7)	23.9	**<0.001** [a]
Severe	32 (38.1)	31 (57.4)	1 (3.3)		
Medication					
Frequency of rescue treatment (%)					
Daily	7 (23.3)	5 (25)	2 (20)		
Weekly	11 (36.7)	7 (35)	3 (30)	0.12	0.74 [a]
< week	30 (35.7)	20 (37)	10 (33.3)		
Rescue and controller treatment	54 (64.3)	34 (63)	20 (66.7)		
ICU admission					
Absent	9 (10.7)	3 (5.6)	6 (20)	4.2	0.4 [a]
Present	75 (89.3)	51 (94.4)	24 (80)		
Number of days					
mean ± SD	3.57 ± 1.96	4.02 ± 2.07	2.63 ± 1.28	376	**0.006** [b]
median (range)	3 (1 – 8)	4 (1 – 8)	2 (1 – 6)		
Frequency of hospitalization					
mean ± SD	4.45 ± 1.97	5.09 ± 2.03	3.30 ± 1.21	386.5	**<0.001** [b]
median (range)	4 (1 – 8)	5 (1 – 8)	3 (1 – 7)		

[a] *=Chi-square test.* [b] *=Mann Whitney U test. Statistical significance at P < 0.05*

Also, Contreras et al.[21] reported that early-onset asthma increases the risk of having obesity at the age of eight two times more than late-onset asthma. In agreement with previous studies, we found that an increased risk of hospitalizations among asthmatic patients in the present study was associated with increased age and obesity. However, age did not rise to the level of statistical significance regarding poor asthma outcomes (p=0.68). Asthma control and severity in children are markedly affected by the BMI status of the patients. The present study demonstrated that obese patients had a significantly higher association with a severe type of asthma. Likewise, poorly controlled asthma was significantly higher among obese patients compared to non-obese ones. Moreover, multivariate regression analysis showed that increased severity of asthma was significantly associated with obesity (OR= 18.06, p=0.045) and higher serum Ig E (OR= 1.040, p=0.001). These results are similar to those reported by Quinto et al. [22] where there was a statistically significant difference in the β-agonist unit dispensing and oral corticosteroid dispensing based on body mass index (BMI) where obese children had 17% more risk of having β-agonist unit dispensing compared to normal-weight children after adjusting for demographics. Although the relation between asthma control and obesity among children is not clearly understood, several hypotheses have been proposed to explain this relation. First, the inflammatory hypothesis suggests that tissue

hypoxia, due to the progressive growth of adipose tissue, leads to release of the pro-inflammatory mediators such as adipokine levels, including leptin, interleukin-6, tumor necrosis factor-alpha, interferon-gamma.

Table 4. Logistic regression analysis of severity of asthma				
Predictors	**Unstandardized Coefficients**		**Odds ratio (95% CI)**	**P value**
	B	**Std. Error**		
(Constant)	-16.485	4.991		**0.001**
Age	0.071	0.173	1.074 (0.766 – 1.505)	0.68
Serum Ig E	0.039	0.011	1.040 (1.017 – 1.064)	**0.001***
Obese *vs.* non-obese	5.231	2.844	18.066 (0.71 – 49.3)	**0.045***

Statistical significance at P < 0.05

Table 5. Linear regression analysis of determinants of hospitalization frequency					
Predictors	**Unstandardized Coefficients**		**Std. Coefficients Beta**	**95% CI**	**P value**
	B	**Std. Error**			
(Constant)	-2.378	1.200			0.051
Age	0.150	0.074	0.213	0.003-0.297	**0.045***
Serum IgE	0.010	0.002	0.495	0.007-0.014	**<0.001***
Obese *vs.* non-obese	1.563	0.450	0.382	0.668-2.458	**0.001***

*ANOVA <0.001, R^2=0.411, *Statistical significance at <0.005*

These mediators lead to reductions in Th2/Th1 cell ratios and eventually result in the reduction of lung function[23,24]. Another explanation is that the disproportionate growth between lung parenchymal size and airway caliber, which is common among obese children, was significantly associated with greater exacerbation frequency[25]. In the present study, obese patients had a higher frequency of ICU admission (p=0.006) and frequency of hospitalization (p<0.001) compared to non-obese ones. Multivariable linear regression analysis was used to assess predictors of hospitalization frequency among asthmatic pediatric patients. Again, the increased risk of

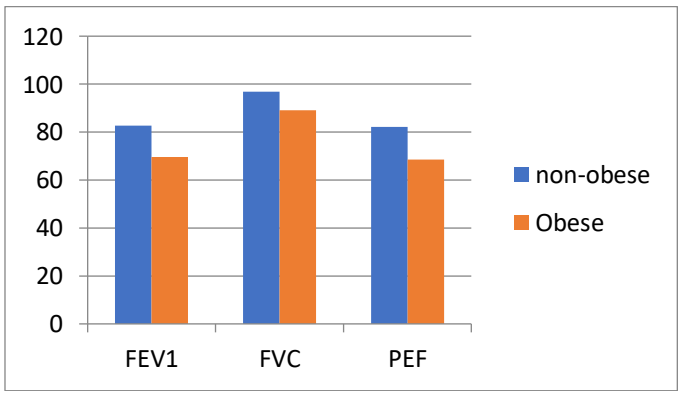

Figure 1. Different spirometry parameters among the two groups (p<0.001)

hospitalization among patients was significantly associated with obesity, where there is an increase in the odds of hospitalization frequency by 1.56 times in obese asthmatic patients compared to non-obese ones (β= 1.56, p=0.001).

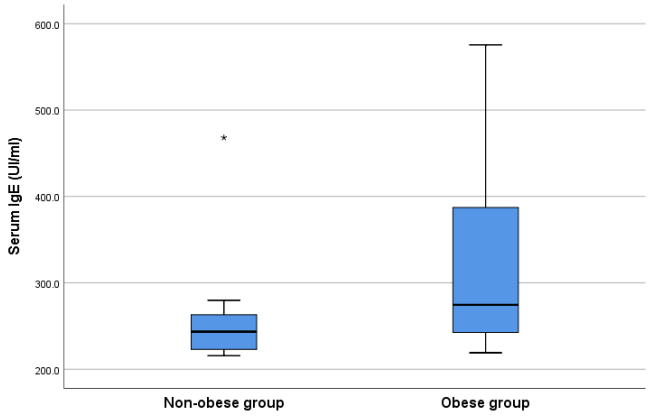

Figure 2 . Serum IgE level among both groups

This is similar to the results of a meta-analysis conducted by Ahmadizar et al. [26] in 2016 that included 46070 asthmatic children and adolescents and concluded that obese children compared with non-obese peers had a small but significantly increased risk of asthma exacerbations that require hospitalization (OR= 1.17, 95% CI: 1.03-1.34). In line with previous studies, Gross et al. [27] found that overweight or obese children were associated with a higher asthma severity (P = 0.021). Moreover, overweight, or obese children had a significantly longer mean length of stay compared with normal weight counterparts (2.75 vs 2.39 days; P <0 .01) with more PICU stays (P= 0.006). Overweight or obese children were significantly associated with higher rates of admission to PICU compared to normal-weight asthmatic children (13.3% vs 8.3%, p= 0.01). There has been a debate regarding IgE levels difference between obese and non-obese patients. Our findings showed that obese asthmatic patients had significantly higher Ig E levels compared to non-obese asthmatic patients (322.43 ± 103.06 vs 250.96 ± 45.67) (p<0.001). This comes consistent with Holguin et al. [28] who found that Ig E levels were significantly higher in obese asthmatics, especially those with early-onset asthma, compared to the non-obese early and late-onset asthmatics. However, other authors suggest that immunoglobulin E level is dependent on the onset of the illness more than his BMI status[28,29], where early-onset asthma is associated with higher Ig E levels and greater bronchial hyperactivity, whereas late-onset asthma is associated with lower Ig E levels and mild form bronchial activity. Overall, for obese asthmatic children, therapeutic strategies should include plans for weight reduction as appropriate lifestyle changes, adherence to dietary guidelines, and increasing exercise for effective weight control and optimal asthma management.

Conclusion

Obesity among asthmatic children and adolescents is linked with more severe asthma exacerbations and more hospitalization frequency. Moreover, lung function

estimations show significant impairment compared to the normal weight counterparts.

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