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IMPACT OF OBESITY ON ASTHMA SEVERITY AND CONTROL IN SCHOOL AGED CHILDREN

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Abstract
Childhood asthma and obesity are significant public health problems. The prevalence of asthma and obesity in children has increased significantly during the past decades. The basis for the relationship between pediatric asthma and obesity is not well established. Our study aimed to find the relation between obesity and bronchial asthma and whether obesity may contribute to more severe asthma symptoms in asthmatic children at Qena University Hospital. This was a cross-sectional study of asthmatic school aged children who were admitted at pediatric department or attended emergency department or the outpatient clinic of Qena University Hospital through the period from MAY 2018 to April 2019.They classified according to BMI to two groups, asthmatic obese and asthmatic non-obese. The included asthmatic children are subjected to full through history, clinical examination and pulmonary function tests. This was a cross-sectional study which was carried out in Pediatric department of Qena university hospital and included 60 asthmatic children with intermittent to severe persistent asthma with age range 6-12 years through the period from MAY 2018 to April 2019 and classified to two groups, 30cases asthmatic obese and 30 cases asthmatic non-obese, based on calculated BMI in both groups. The patients were diagnosed according to the global strategy for asthma management and prevention classification. The mean age in asthmatic obese patients was (8.94±1.99) versus (9.13±1.97) in asthmatic non-obese group with no significant difference between them (p-value =0.707). The percentage of moderate persistent asthma was statistically significantly higher in asthmatic obese than asthmatic non-obese group (53.3% versus 26.7%, p-value= 0.035), respectively. 13.3% of asthmatic obese had severe persistent asthma versus 0% in asthmatic non-obese group (p-value=0.038).46.7%of the asthmatic obese children received high dose of steroids versus 10%of asthmatic non-obese with statistically significant difference (p value =0.001). The mean numbers of emergency visits in asthmatic obese were significantly higher than that in asthmatic non-obese (5.9±2.66versus 3.93±1.6), (p-value= 0.001), respectively. FEV1, FVC, FEV1/FVC, were not significantly different in asthmatic obese patients compared with asthmatic non-obese (p-value =0.742, 0.849, 0.751, respectively). Obesity was associated with significantly more severe asthma symptoms together with poor asthma control. Pulmonary function tests were not affected by increased BMI.

Keywords: *Bronchial Asthma, Obesity, Children, School Aged, BMI.*

I. INTRODUCTION

Asthma and obesity are concurrently at historic high levels in pediatric populations. These two public health epidemics share risk factors (e.g., poverty and physical inactivity); asthmatic children also may be at higher risk for obesity due to reduced exercise capacity. Mounting evidence suggests, however, that obesity independently contributes to the incidence and severity of asthma in children and adults. Although controversy persists regarding the exact nature of the relationship, several mechanisms that potentially mediate the relationship between gastro esophageal reflux, and adipose-induced inflammation (Michelson, 2009).

The parallel rise in prevalence of both disorders and the coexistence of both asthma and obesity in many children has led to interest in the relationship between the two epidemics. In the past decade, the relationship between asthma and obesity has been explored extensively but, in most areas, the data is inconsistent and there are few clear answers (Story, 2007).

Obesity may also be associated with asthma severity and/ or poor asthma control in children and adults. Studies have shown that obese patients with asthma are often prescribed a greater number of β-agonists and oral corticosteroids and have more frequent emergency department visits and hospitalizations for asthma exacerbations than their normal- weight counterparts (Black, 2013).

II. METHODS

This was a cross-sectional study of asthmatic school aged children who were admitted at pediatric department or attended emergency department or the outpatient clinic of Qena University Hospital through the period from MAY 2018 to April 2019. The study was carried out on 60 asthmatic patients divided into 2 groups (30 asthmatic obese patients and 30 asthmatic non obese patients matched in age and sex) classified according to BMI {BMI= weight/height2 (kg/m2)}, into:

Normal weight: BMI is equal to or greater than the 5th percentile and less than the 85th percentile for age and gender.

Overweight: BMI is at or above the 85th percentile but less than the 95th percentile for age and gender.

Obese: BMI is at or above the 95th percentile for age and gender (Gallagher et al., 2000).

Inclusion criteria: -

All patients were diagnosed with bronchial asthma according to GINA (2010).

Age :between 6 and 12 years

Both males and females.

Exclusion Criteria: -

Age below 6 years or above 12 years.

Patient with acute chest infection.

Chronic chest disease other than bronchial asthma.

Patient with immunodeficiency.

Cardiac disease.

Refusal to participate in the study.

All patients subjected to the following: -

Medical history: -

Symptoms: cough, wheezing, shortness of breath, chest tightness, or sputum production.

Pattern of symptoms:

Perennial, seasonal, or both

Continual, episodic, or both

Diurnal variations

Onset, frequency, and duration (number of days or nights, per week or month).

Family history: history of asthma, allergy, rhinitis, sinusitis, or obesity in close relatives.

Clinical examination: -

Vital signs recording.

Weight and height measuring.

Chest examination in detail.

Other systems examination.

Investigations: -

The following tests were carried out:

CBC and differential count with special concern on eosinophil: (Cell Dyn 1800-Abbott diagnostics, Germany).

Total IgE was performed using commercially available sandwich enzyme-linked immunosorbent assay (ELISA) kits, supplied by Chongqing Biospes Co., Ltd (Chongqing, People's Republic of China) with the catalog number: BYEK2772, using microplate ELISA reader (EMR -500, USA). (Hassan et al 2018 and Kim et al 2013).

Chest x rays: using Philips medical systems D-22335 Hamburg, Germany.

Pulmonary function tests:

This was done by spirometry (Fukuda Denshi, Spirosift SP5000). Spirometer is a simple volume record consisting of drum (air chamber) inverted over a chamber of water. The drum is counter balanced by a weight and is attached by pulley to a pen that writes on a paper attached to a rotating drum. A tube connects the mouth with the gas chamber. When one breathes into the tube, air enters the chamber from the lungs and the drum rises. Downward pen defection represents expiration and upward pen defection represents inspiration. It comprised the following Spirometric Parameters:

Forced vital capacity (FVC)

The maximum volume of gas that can be forcefully expelled after maximal inhalation (Rupple, 1998).

Forced expiratory volume in the first second (FEV1)

The volume of gas expired in a given time interval (in the first second) from the beginning of the FVC maneuver (Yur Dakule et al., 2005).

The FEV1 is the most widely used spirometric parameter, particularly for the assessment of airway obstruction. Also, distinction between obstructive and restrictive causes of reduced FEV1 to the forced vital capacity as FEV1/ FVC ratio (Wagner, 1992).

FEVı/ FVC

The ratio between the forced expiratory volumes in the first second to the forced vital capacity, expressed as a percentage. Results of spirometry were expressed as a percentage of predicted value adjusted for gender, age, and height. The FVC, FEV1 were considered abnormal if they were less than 80% of the normal predicted value. The FEV1/FVC ratio was considered abnormal if less than 75% (Miller, MR et al., 2005).

STATISTICAL ANALYSIS

Data were analyzed using Statistical Package for Social Sciences (SPSS) software program (version 26). Qualitative variables were recorded as frequencies and percentages and were compared by chi-square test. Quantitative measures were presented as means ± standard deviation (SD). Correlations between variables were done using spearman correlation coefficient. P-values less than 0.05 were considered as statistically significant.

III. RESULTS

This was a cross-sectional study that included all asthmatic children who were either admitted to paediatric department or attended emergency department or the outpatient clinic of Qena University Hospital through the period from May 2018 to April 2019. Clinical evaluation was done on 60 asthmatic cases during the period of the study. Regarding sex distribution of the studied group, 55% of the studied group were males versus 45% were females with no significant difference (p-value=.438) (table 1).

Table1: Sex distribution of the studied group.

variable		n (%)	p-value
Sex	male	33 (55%)	0.438
	female	27 (45%)	

Regarding socio-demographic data, the mean age for asthmatic obese group was (8.94±1.99) compared to (9.13±1.97) in asthmatic non-obese group with no significant difference between 2 groups (p value =0.707). Regarding sex distribution, 53.3% of asthmatic obese cases were males compared to 56.7% in asthmatic non- obese group with no significant difference between them (p-value = 0.795).

Regarding residence, 46.7% of asthmatic obese group came from rural areas compared to 50% in asthmatic non-obese group with no significant difference between them (p-value=0.796). Also, there was no significant difference between two groups regarding the percentage of residence in urban areas (53.3% vs 50%, p=0.796, respectively). There were no significant differences between two groups regarding socioeconomic standards, maternal educations, number of siblings, history of tobacco exposure, consanguinity, nutritional history and modes of delivery , (p-values = 0.436, 0.071, 0.268, 0.592, 0.297, 0.371, 0.317, respectively).

Concerning family history of obesity, asthmatic obese group showed significantly higher percent of family history of obesity when compared to asthmatic non-obese group (36.7% vs 0%, p-value = 0.000 respectively).Also, family history of obesity &asthma was higher in asthmatic obese than asthmatic non-obese (10%versus 0%) with statistically significant difference between 2 groups (p value =0.005). There was no significant difference between two groups regarding family history of asthma (p-value = 0.417) (table 2).

Figure (1): Asthma degree distribution among the studied groups.

Variable		Asthmatic obese group (n=30)	Asthmatic non-obese group(n=30)	P-value
Age (mean±SD)		8.94±1.99	9.13±1.97	0.795
Sex n (%)	Male	16 (53.3%)	17 (56.7%)	0.795
	Female	14 (46.7%)	13 (43.3%)	0.795
Residence n (%)	Urban	14 (46.7%)	15 (50%)	0.796
	Rural	16 (53.3%)	15 (50%)	0.796
Socioeconomic status n (%)	low	12 (40%)	15 (50%)	0.436
	moderate	18 (60%)	15 (50%)	0.436
Family history n (%)	No	9 (30%)	18 (60%)	0.121
	asthma	7 (23.3%)	12 (40%)	0.417
	obesity	11 (36.7%)	0 (0%)	0.000*
	Obesity &asthma	3 (10%)	0 (0%)	0.005*
Maternal education n (%)	educated	12 (40%)	19 (63.3%)	0.071
	Non educated	18 (60%)	11 (36.7%)	0.07 1
Consanguinity n (%)	+ve	15 (50%)	19 (63.3%)	0.297
	-ve	15 (50%)	11 (36.7%)	0.297
Nutritional history n (%)	BF	19 (63.3%)	15 (50%)	0.297
	Formula	6 (20%)	10 (33.3%)	0.371
	BF+formula	5 (16.7%)	5 (16.7%)	1.00
Modeof delivery n (%)	NVD	7 (23.3%)	4 (13.3%)	0.317
	CS	23 (76.7%)	26 (86.7%)	0.317
Tobacco exposure n (%)	yes	20 (66.7%)	18 (60%)	0.592
	no	10 (33.3%)	12 (40%)	0.592
N. sibling(mean±SD)		3.13±1.48	2.73±1.29	0.417

Table (2): Socio-demographic characteristics Comparison among the studied groups.

BF: breast feeding, N.sibilings: number of siblings, NVD: normal vaginal delivery, CS: cesarean section.

Regarding health status characteristics of the studied groups, the co-morbid conditions associated with asthma in the studied groups showed no significant difference between two groups regarding the percentage of GERD (10% in asthmatic obese group vs 6.7% in asthmatic non-obese group, p=0.640). Also, there were no significant differences between asthmatic obese and asthmatic non-obese group regarding the percentage of allergic rhinitis (13.3% versus 13.3%, p= 1.00, respectively), eczema (3.3% versus 3.3%, p=1.00, respectively), atopic dermatitis (10% versus 0%, p=0.076, respectively), urticaria (3.3% versus 6.7%, p=0.554, respectively), and food allergy (6.7% versus 10%, p=0.643, respectively). There were no clinical history of co-morbidities or allergic conditions detected in 53.3% in asthmatic obese and 60% in asthmatic non-obese groups with no statistically significant differences between them (p=0.592). Regarding the frequency of degrees of asthma in both groups(figure 1), the percent of intermittent asthma was (0%) in asthmatic obese group compared to (30%) in asthmatic non-obese group, (P=0.001).The Percent of mild persistent asthma was (33.3%) in asthmatic obese group compared to (43.3%) in asthmatic non -obese group with no statistically significant difference between them (p=0.426). on the other hand, the percentage of moderate persistent asthma was statistically significantly higher in asthmatic obese group (53.3%) than that in asthmatic non-obese group (26.7%), (p- value=0.035).The percentage of severe persistent asthma was statistically significantly higher in asthmatic obese group (13.3%) than that in asthmatic-non obese group (0%), (P- value=0.038). There was no significant difference between asthmatic obese and asthmatic non-obese regarding duration of asthma in years (p=0.944).The mean numbers of each of night awakenings per week, absence's day from school per month, doctor visits per month, seasonal exacerbations per one year, emergency visits per one year were significantly higher in asthmatic obese group than that in asthmatic non-obese group (3.13±2.08 vs 1.1±.995, 5.9±3.055 vs 1.87±1.634, 2.13±1.383 vs 73±.828, 2.27±1.461 vs 1±0.91, 5.9±2.66 vs 3.93±1.6, respectively) (p-values= 0.001, 0.001, 0.001, 0.001, 0.001, respectively).On the other hand, there were no statistically significant differences between two groups regarding mean numbers of each of hospital admission perone year, PICU admission perone year and oxygen saturation at admission (p= 0.397, 0.054, 0.055, respectively).Regarding the dose of steroids which received by the patients, 63.3% of asthmatic non-obese group received low dose of steroids which was statistically significantly higher than that of the asthmatic obese group (13.3%), (p= 0.001). on the other hand, 46.7% of asthmatic obese group received high doses of steroid which was statistically significantly higher than that in asthmatic non-obese group (10%), (p-value=0.001).There was no significant difference between two groups regarding the percentage of patients received moderate doses of steroids (p=0.237).Regarding compliance of therapy, 30% of asthmatic obese were compliant compared to 83.3% in asthmatic non-obese with statistically significant difference(p=0.001).The mean eosinophilic percentage in asthmatic obese group was significantly higher than that in asthmatic non-obese group (10.67%±6.46 vs 5.87%±3.17, p-value=0.001, respectively). On the other hand, there was no significant difference between two groups regarding the mean level of IgE (99.83±233.81 vs 114.5±243.37), p-value=0.813), respectively. (Table 3).

Pulmonary function tests showed no significant differences between asthmatic obese and asthmatic non-obese groups regarding means of each of FEV1 (61.33%±5.79 vs 60.87%±5.11, p=0.742), FVC (83.83%±3.33 vs 83.67%±3.39, p=0.849) and FEV1/FVC (71.93%±4.8 vs 71.57%±4.07, p=0.751), respectively (table 4).

Regarding correlations between BMI and grades of asthma, duration of asthma and emergency number of visits per 1 year, there were significant positive correlations between BMI and each of grades of asthma and emergency number of visits per one year {(R=0.302, P=0.019), (R=0.377, P=0.003), respectively}. On the other hand, there was no significant correlation between BMI and duration of asthma (R=0.377, P=0.003) (table 5).

Table (3): health status characteristics Comparison among the studied groups #.

Variable	Asthmatic obese group (n=30)	Asthmatic non-obese group(n=30)	P-value

Comorbidities at base line& other types of allergy n (%)	GERD	3 (10%)	2 (6.7%)	0.640
	allergic rhinitis	4 (13.3%)	4 (13.3%)	1.00
	eczema	1 (3.3%)	1 (3.3%)	1.00
	atopic dermatitis	3 (10%)	0 (0%)	0.076
	urticaria	1 (3.3%)	2 (6.7%)	0.554
	food allergy	2 (6.7%)	3 (10%)	0.643
	no	16 (53.3%)	18 (60%)	0.592
Grades of asthma n (%)	intermittent	0 (0%)	9 (30%)	0.001*
	mild persistent	10 (33.3%)	13 (43.3%)	0.426
	moderate persistent	16 (53.3%)	8 (26.7%)	0.035*
	severe persistent	4(13.3%)	0 (0%)	0.038*
Duration of asthma in years		4.03±1.85	4.07±1.82	0.944
No. of night awakenings per week		3.13±2.08	1.1±.995	0.001*
No. of absence's day from school per month in days		5.9±3.055	1.87±1.634	0.001*
No. of doctor visits per month		2.13±1.383	0.73±.828	0.001*
No. of seasonal exacerbation per one year		2.27±1.461	1±.91	0.001*
No. of emergency visits per one		5.9±2.66	3.93±1.6	0.001*

GERD: gastro-esophageal reflux, PICU: pediatric intensive care unit, IgE: immunoglobulin E. #: Data is expressed as number (%) and (mean ±SD).

Table 4: pulmonary function tests Comparison among the studied groups. (FVC) forced vital capacity, (FEV1) forced expiratory volume in the first second.

	Asthmatic obesegroup (n=30)	**Asthmatic non-obese group(n=30)**	**P-value**
	Mean±SD	**Mean±SD**	
FEV1 (%)	**61.33%±5.79**	**60.87%±5.11**	**0.742**
FVC (%)	**83.83%±3.33**	**83.67%±3.39**	**0.849**
FEV1/FVC (%)	**71.93%±4.8**	**71.57%±4.07**	**0.751**

Table 5: correlation between BMI and grade of asthma, duration of asthma and emergency number of visits per 1 year.

		Grades of asthma	Duration of asthma	Emergency No. of visits in 1 year
BMI	Spearman Correlation	0.302**	0.112	0.377**
	P-Value	0.019	0.394	0.003

IV. DISCUSSION

Asthma is a chronic inflammatory disorder of the airways in which many cells play a role. The chronic inflammation causes an associated increase in airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, and coughing particularly at night or in early morning (Sharma, 2006). Asthma is the most prevalent chronic illness of childhood and has a major impact on lifestyle (Orenstein, 2002).A number of prospective studies have shown that weight gain can precede the development of asthma (Schaub &Von Mutius, 2005). There is evidence of a positive association between asthma and obesity in adults and children (Guler et al., 2004).

In our study males, represented 55% of total asthmatic cases and females represented 45%. with no significant difference between two percentages, (p-value=0.438).There were no significant differences between asthmatic obese and asthmatic non-obese regarding means of age and sex (p- value=0.707, 0.795) respectively. This was in agreement with Esfandiar et al 2016 who found that there was no significant relation between sex and asthma (p-value=0.559). In contrast to our results, Menezes et al., 2007 found that boys were 38% more likely to wheeze than girls.

Regarding degrees of asthma severity, asthmatic obese group showed significant higher percentages of both of moderate persistent and severe persistent asthma than that of asthmatic non- obese group (p=0.035and 0.038, respectively). On the other hand, asthmatic non-obese showed significant higher percentage of intermittent asthma than that of asthmatic obese group (p=0.001).This was in agreement with Lang, 2012 who reported that obese children were more likely to be given the diagnosis of severe persistent asthma compared to normal/overweight children. Contrary to our results, Tantisira et al., 2003 found that higher BMI in childhood was not associated with increased asthma severity.

In our study, asthmatic obese group showed significant higher means of numbers of night awakenings per week, absence's day from school per month and doctor visits per month than that of asthmatic non-obese group (p-value=0.001, 0.001, 0.001, respectively). In agreement with our results, Yuksel, 2012 found that the mean asthma symptom score was significantly higher in the obese children with asthma than in the non-obese children with asthma (10.9±2.8 vs. 8.2±2.9; P=0.001). Contrary to our result, Tantisira et al., 2003 found that increasing body mass was not associated with increasing asthma symptoms.

Our study showed that the mean number of seasonal exacerbations per one year was statistically significantly higher in obese group than that of non- obese group (p value =0.001). In agreement with our results, Quinto, 2011found that overweight and obesity in children is associated with increased risk of asthma exacerbations. Contrary to our results, Lang, 2012, found that obesity did not appear to be a risk factor for asthma exacerbation.

In our study we reported significant higher means of numbers of emergency visits per one year in asthmatic obese group than that of asthmatic non- obese group, (p value =0.001). In agreement with our results, Vargas et al.,2007reported that an increased BMI was associated with more emergency department visits. In contrast to our results, Quinto, 2011 found that there was no association found between overweight and obese children and increased risk for emergency department visits.

Regarding serum IgE level, our study shows that there is no statistically significant difference between two groups (P-Value=0.813). This was in agreement with Kim, 2008 who reported that there were no differences in atopy parameters, such as serum total IgE, among the normo-weight, overweight, and obesity groups. In contrast to our results, CASTRO-RODRÍGUEZ, 2001 reported that a higher percentage of obese children having bronchial hyper reactivity detected by increasing IgE level compared with non-obese children.

In our study, regarding eosinophil%, asthmatic obese showed significant higher levels than that of asthmatic non-obese group (p-value=0.001). Similar to our results, Grotta, 2013 found that there is increased eosinophilic activity (chemotaxis and adhesion) in atopic obese children and adolescents compared with non-obese volunteers (p-value =0.0007). In contrast to our results, Tantisira et al., 2003 found that there was no significant association between eosinophil and BMI (P-Value= 0.06).

In our study we reported that (46.7%) of asthmatic obese group used high doses of steroids versus (10%) in asthmatic non-obese group, (p=0.001). on the other hand, (63.3%) of asthmatic non-obese group used low doses of steroids vs (13.3%) in asthmatic obese group, (p=0.001). Thiswas in agreement with Quinto, 2011who found that being overweight and obese as a child is associated with increased oral corticosteroid dispensing. Contrary to our results, Lang, 2012 found that obesity may not be a major contributor to treatment burden and the health-care costs associated with daily controller therapy.

In our study, no significant difference between two groups regarding FEV1, FVC, FEV1/FVC, p-value were (0.742, 0.849, 0.751, respectively). This was in agreement with Baek, 2011 who found that there were no significant differences in FEV1, FVC, or FEV1/FVC ratio between the obese subjects with asthma and normal- weight subjects with asthma. Contrary to our results, Spathopoulos, 2009 found that pulmonary function in children with obesity defined by BMI percentile is characterized by a reduction in most spirometric indices such as FEV1, FVC, and FEV1/FVC.

V. CONCLUSION

Children with obesity and asthma are associated with more severe asthma symptoms, frequent and severe exacerbations, poor asthma control with decreased response to inhaled steroids and this in turn is affecting the quality of life of these children. Spirometricpulmonary function is not affected by increase BMI.

VI. RECOMMENDATIONS

Further longitudinal studies on larger sample size are required to evaluate obesity/asthma relationship with further insights on pathogenesis, of obesity on asthma severity and pulmonary functions with determination of treatment strategies in this group of asthmatic children.

Further longitudinal studies are also required to determine the impacts of decease body weight as an important step of treatment and improving quality of lifestyle in asthmatic obese children.

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