The relation between simple obesity, Asthma and the serum level of interleukin-6 (IL-6) In Egyptian Children

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Abstract: Objectives: obesity is considered a risk factor for asthma, in spite of the mechanism of connection between the two conditions isn't clear. In this study we investigated the relationship between asthma, simple obesity and serum level of interleukin 6 (IL6). Patients and Methods: 51 Egyptian child, attending chest and allergy out patient Pediatric Clinics Benha University hospital aged from 3 to 15 years old. From June 2010 to June 2011. the studied group divided into 34 asthmatics (cases) and 17 healthy non asthmatic (control). Asthmatic and control subjects were divided into 2 main sub groups: obese and non obese. We did for all subjects: complete history taking, anthropometric measures (weight, height, calculation of BMI, Mid arm circumference), complete blood picture (CBC) including eosinophilic%, peak expiratory flow rate (PEFR) as one of pulmonary function test, measurement of serum interleukin 6 (IL.6). Results: IL.6 serum level was in asthmatic patients in general more than its level in controls. In obese asthmatics the IL.6 level was higher than non obese asthmatics and the same between obese and non obese controls. Increase IL-6 level was related to increase BMI percentiles. Increase IL-6 level and BMI percentiles related to increase the severity of asthma. PEFR is lower in asthmatics than the controls. PEFR is more lower with the severity of asthma. Conclusion: there is a relationship between IL.6 serum level and simple obesity and asthma. We found that obesity may precipitate asthma and so weight reduction of obese asthmatic patients may be helpful in the treatment of asthma.

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1. Introduction

Bronchial asthma is one of the most common pediatrics chronic disease that is responsible for significant morbidity; school absenteeism and mortality ***(Akinbami et al., 2006)***.

Obesity becomes a serious heath problem world wide and increase during last decade due to changes in eating habits and decrease physical activity ***(Popkin et al., 2004 and Shore et al., 2005).***

Asthma is also on the increase as a result of industrialization from urbanization ***(GINA 2010).***

Several recent review articles have concluded that there is a positive association between obesity and asthma ***(Beuther et al., 2006)*** but the under lying mechanisms have not yet been established.

Many studies suggest that weight loss and weight gain may have an effect on the clinical course of asthma ***(Ronmark et al., 2005, Schuab et al., 2005 and Shore, 2007).***

Several mechanisms have been postulated ***(Shore, 2008).*** Firstly obesity and asthma may share common genetic and environmental etiologies. Genetic and environmental factors may increase the risk of obesity concurrently with asthma ***(Mai Max et al., 2008).*** Obesity may increase the risk of asthma through its effects on other disease process e.g. obesity is a risk factor for sleeping disordered breathing and gastro-esophageal reflux disease ***(HAMPEL et al., 2006),*** and these two diseases are associated with an increased risk for asthma ***(HANCOX et al., 2006).***

Then morbid obesity can reduce lung volume and airway diameter and increase asthma via mechanical mechanisms ***(Bauther et al., 2006).*** Obesity is characterized by increase in the serum concentrations of cytokines, chemokines, acute phase proteins and energy regulating hormones including leptin, IL-6, TNF-alpha and others ***(BERG et al., 2005 and Schere et al.,2006).*** These mediators are produced by adipocytes and in general called adipokines,they may alter T helper1 (Th I)& T helper 2 (Th 2) balance, immune tolerance, lung development, air way smooth muscle and airway responsiveness which are associated with asthma development***(Hersoug et al., 2007)***.

Also these inflammatory cytokines play a secondary role in producing asthma, these cytokines contribute to IgE production, sub epithelial fibrosis and airway remodeling which are primary in the pathogenesis of asthma.

In this study we investigated the relation between asthma, simple obesity and serum IL-6 level in children aged from 3to15 years old.

We compared between obese, non obese asthmatics and obese, non obese controls who are not asthmatic regarding to IL-6 level.

2. Patients and Methods:

Our data collected from 34 Egyptian asthmatic children were attending Pediatric Chest and Allergy out patient clinics, Benha University hospital. They were 20 males and 14 females their ages ranged from 4 to 15 years with mean age (8.3±3.1).

Seventeen matched apparently healthy children without history of asthma or any other a topic diseases were studied as controls. They were 9 males, 8 females their ages ranged from 3 to15 years with a mean age (7.6 ± 3.7). This study was carried out over a period of 12 months from June 2010 to June 2011.

The studied cases were classified in to:

Obese: 17 cases (50%) & non obese: 17 (50%) [according to BMI age percentiles].

Mild intermittent asthma: 5cases (14.7%) & mild persistent asthma :8 (23.5%)& moderate persistent asthma: 10 (29.4%) and sever: 11 (32.4%) [according to severity of asthma*].(GINA, 2010).*

Un controlled asthma: 14 cases (41.2%) & partially controlled:10 (29.4%) and controlled: 10 (29.4%) [According to level of asthma*](GINA, 2010).*

All cases were subjected of full history taking, clinical examination, anthropometric measurements (weight, height, BMI and put on BMI age percentiles and mid arm circumference), CBC with differential Leukocytic count, peak expiratory flow rate (PEFR) (expected for age & sex) and measurement of serum IL-6 level.

The measurement of serum IL-6 level done for all cases and controls by ELISA "Enzyme- Linked Immunosorbent Assay) Technique.

Samples of serum were collected after centrifuging blood samples for 10 min, serum was immediate separated into aliquots and stored at -20 until essay.

The standard curve is used to determine the amount of IL-6 in an unknown sample. The standard curve is generated by plotting the average O.D (Optical- Density) (450mn) obtained for each of the standard concentration on the vertical (γ) axis versus the corresponding IL-6 concentration (pg/ml) on the horizontal (x) axis.

(NB: cut off value = mean ± 3SD).

The collected data were tabulated and analyzed using SPSS version 16 soft ware. Categorical data were presented as number and percentages while quantitative data were expressed as mean ± SD (standard deviation) and range. Chi square test (X^2), student (t) test, ANOVA (F) fest and spearman's correlation coefficient were used as tests of significant). [P value > 0.05 insignificant& P < 0.05 significant and P < 0.01 highly significant].

3. RESULTS:

In our study the asthmatic group consisted of 34 patients they were 20 males and 14 females, ratio 1.3 : 1, mean age (8.3 ±3.1) and 17 controls were 9 males and 8 females with mean age (7.6 ± 3.7). The asthmatic patients and the controls were divided according to BMI age percentiles to 17 obese asthmatics and 6 obese controls where the BMI age percentiles were ≥ 95th and 17 non obese asthmatics and 11 non obese controls where the BMI age percentiles were < 95th.

Table (1): Mean of serum IL-6 level among obese & non obese controls and asthmatics

	Mean ± SD		P	Mean ± SD		P
	Non-obese controls (n=11)	Obese controls (n =6)		Non-obese asthmatics (n = 17)	Obese asthmatics (n = 17)	
Serum I.L-6 Level (pg/ml)	3.43±2.7	11.12±5.8	< 0.01	22.5±5.6	28.69±9.7	< 0.05

IL-6: Interlukine-6

Table (2): Statistical comparison between obese controls and obese asthmatic according to mean serum IL-6.

IL-6(pg/ml) Group (obese)	N	Mean	Std. Deviation	St."t"	P
Control group	6	11.12	5.8	-4.1	<0.001
Asthmatic group	17	28.69	9.7		

IL-6: Interlukine-6

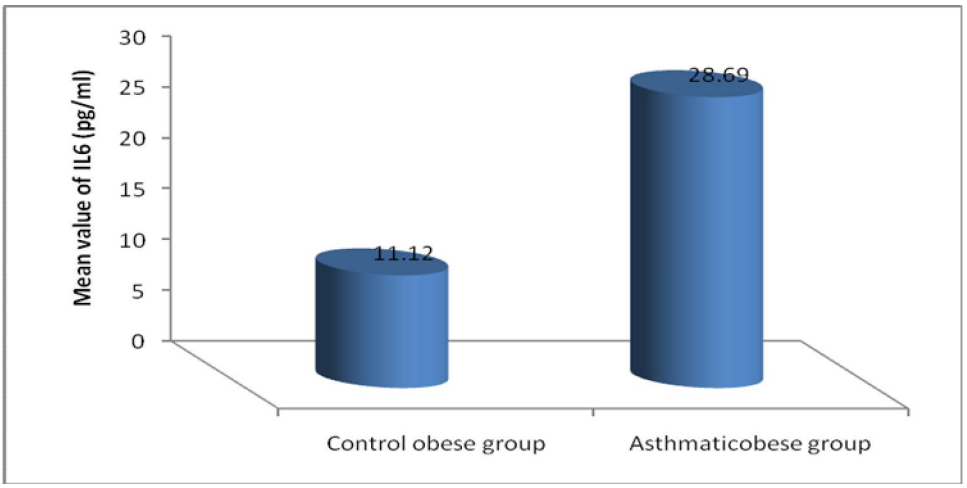

Figure (2): Statistical comparison between obese controls and obsess asthmatic according to serum I.L. 6

Table (3): Correlation between mean serum IL-6 level and BMI.

With \ IL-6	r	P
BMI	**0.357**	**<0.05**

BMI: Body mass index IL-6: Interlukine-6

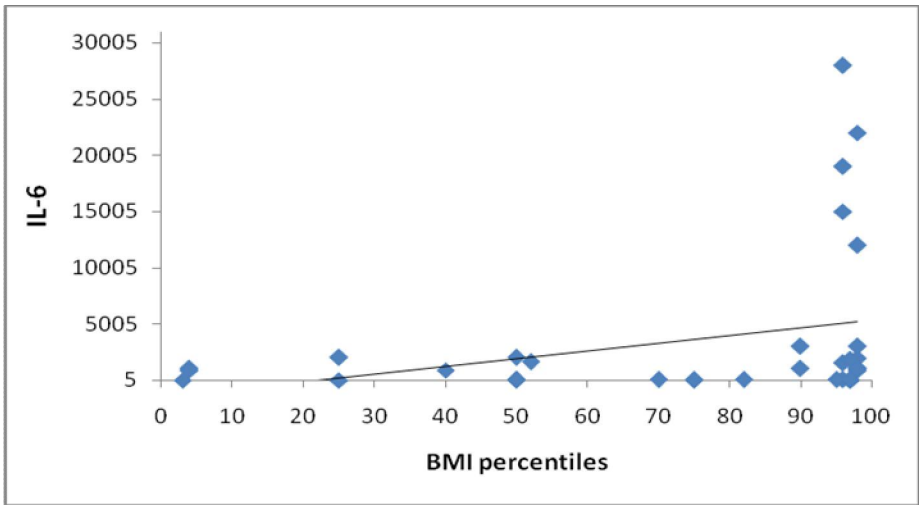

Figure (3**): correlation between serum IL-6 level and BMI.**

Table (4): The statistical difference between obese asthmatics non obese asthmatics according to (PEFR expected for age & sex)

Group	PEFR			
	N	Mean	Std. Deviation	St "t" &P
Obese asthmatic	**17**	**24.1**	**11.3**	**4.01 & <0.001**
Non obese asthmatic	**17**	**38.0**	**8.8**	

Table (5): Spearman's correlation coefficient between severity of asthma and some variables.

Severity of asthma / variables	R	P
Age	**-0.24**	**>0.05**
BM I	**0.618**	**<0.001**
Eosinophils%	**0.044**	**>0.05**
PEFR	**-0.969**	**<0.001**
IL-6	**0.653**	**<0.001**

BMI: Body mass index IL-6: Interlukine-6 PEFR: Peak expiratory flow rate

In table (1) the relation done between obese and non obese controls and asthmatics regarding mean serum IL.6 level, there's statistical significant difference between obese, non obese controls where it was higher in obese controls than non obese one (**P< 0.05**), and for obese and non obese asthmatics there is significant statistical difference (**P < 0.05**), the level was in obese asthmatic (mean **28.69±9.7)** higher than non obese one (mean **22.5±5.6**).

In table (2) shows the higher level of IL-6 among obese asthmatics (mean **28.69±9.7**) than obese controls(mean**11.12 ±5.8).**

with high significant statistical difference (P < 0.001).

In table (3): there is significant statistical increase in mean serum level of IL-6 with increase BMI (**P< 0.05**).

Table (4) shows that PEFR (expected for age sex) in obese asthmatics is lower than that of non obese asthmatics and there's high statistical significant difference. **(P value <0.001).**

In table(5)in the present study: the correlation between severity of asthma and some variables shows statistical difference between increase BMI , PEFR and mean serum IL-6 level and the severity of asthma.

4. Discussion

Most cross sectional and prospective studies in children support a link between obesity and asthma ***(Chinn, 2006),*** in addition most prospective studies in children show that obesity precedes the development of asthma ***(Flaherman et al., 2006).***

Most prospective studies suggest many possible mechanisms for the relationship between asthma and obesity include airway inflammation mechanical changes, changes in airway hyper-responsiveness, and changes in physical activity and diet ***(Beuther et al., 2006, Lucas et al., 2008 and Pianosi and Davis, 2008). Von et al. (2005)*** concluded that the effects of increased BMI on asthma could be mediated by mechanical properties of the respiratory system associated with obesity or by up-regulation of inflammatory mechanisms rather than by allergic eosinophilic inflammation of the airway epithelium.

Our study found significant difference in the **IL-6 concentration** between obese asthmatic and non obese asthmatics (P < 0.05) this is agreed which what ***Canoz et al., 2008*** concluded that the level of serum IL-6 is higher in obese asthmatics than the other group. Also the level of IL-6 founded in our study higher in obese controls than the non obese one the same as ***Canoz et al., 2008*** said.

In our study the correlation between **IL-.6 level and BMI** shows higher significant level of IL-6 with increasing BMI , the same result said by ***Park et al.,2005*** due to increase adipose tissue which responsible for release of may inflammatory cytokine include IL-6 and tumour necrosis factor alpha .

In this presented study we found that there was high statistical significant difference between obese asthmatic than obese control regarding to **IL-6 level** (P < 0.05) and this agreed with ***Guler et al., 2010*** studies results, where the mean serum IL-6 level were high among obese asthmatics.

Bronchial asthma is characterized by reversible airway obstruction. Pulmonary function tests are a useful way to objective measurement of the degree, location and reversibility of airway compromise in asthmatic children ***(GINA, 2010).*** In the present study of asthmatic patients it was found that obese asthmatics have lower lung functions than non- obese asthmatic, **mean PEFR** in obese asthmatics 24.1 ± 11.3 Liter/sec while in non-obese asthmatics 38 ± 8.8 (p < 0.01). ***Fung et al.(1990)*** reported that there is evidence that obesity is associated with lower lung function, also ***Pelosi et al. (1998)*** found the same results. ***Stenius et al.(2000)*** demonstrated that obesity worsen lung function and improvement of pulmonary function by weight reduction was observed. ***Tantisira et al.(2008)*** concluded the same resultes.

Most studies also found that the obesity increase clinical severity of asthma ***(Matricard et al., 2007*)**, and that agreed with what our study founded where the severity of asrhma was increased with increasing **BMI**(p <0.001). In our study also found the significant lowering in **PEFR** with the severity of

asthma and this agreed with what ***von et al., 2001*** said.

Kim et al. (2008) concluded that increase level of cytokins including **IL-6 level** play a role in increase severity of the asthmatic symptoms and signs and this agreed with our study which found high significant levels of IL-6 among the sever asthmatic children.

Conclusion:

It's obvious that there was a strong relation- ship between asthma and obesity with regards serum IL.6 level. A higher degree of serum IL-6 level were presented in the asthmatic patients than that of the controls, similarly a higher degree of serum IL-6 level was observed in obese participant compared of those with normal weight. These values were highest in obese asthmatic than the others. So as a result, these cases should be encouraged to loss weight. Also we must take care from the dietary habits and life style to avoid gaining weight .we need also further studies in order to better demonstration and clarify the relationship between asthma and obesity.

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