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The Relation Between Serum Adiponectin Level, Body Composition And Asthma Severity In Obese Asthmatic Children.

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ABSTRACT

In children, both obesity and asthma are increasing concomitantly with serious effects on quality of life and health. is to investigate the relation between serum adiponectin, CRP, IL- 6 levels and body composition parameters in obese asthmatic children and its effect on asthma severity. Cross-sectional case-control study was conducted on 30 non-obese asthmatics, 30 obese asthmatics from children attending allergy clinic at Abu-El Rish Pediatric Hospital, and 30 healthy controls. Complete history, clinical examination, anthropometric measurements and body composition parameters were taken. Serum adiponectin, CRP and IL6 levels were estimated using ELISA kits. Obese asthmatics showed highly significant increase in serum IL6 and CRP and highly significant decrease in serum adiponectin level compared to non-obese and control groups ($p< 0.005$ in both). In the obese asthmatic group, there was a negative significant correlation between adiponectin & both fat % and impedance ($p<0.05$), while there was a positive significant correlation with FFM ($p<0.05$). BMI and serum adiponectin level were found to be significant predictors for the severity of asthma in obese asthmatics ($p<0.01$ and 0.05). ROC curve revealed that adiponectin level is sensitive test (86.8 %) in detecting the severity of asthma in obese asthmatics. Serum adiponectin level is a strong sensitive test in detecting the severity of asthma in obese asthmatics.

Keywords: asthma, obesity, children, adiponectin, CRP, IL6

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INTRODUCTION

Obesity and asthma are major public health problems affecting large numbers of children and young adults across the globe[1-2]**.** In Egypt, the prevalence of bronchial asthma was reported to be 7.7% among school children [3]**.** Meanwhile, an increasing rate of overweight and obesity in children and adolescents was reported [4]**.**

Obesity is considered as a pro-inflammatory status that is associated with chronic low-grade systemic inflammation in obese individuals [5-6]. Multiple studies have identified significantly elevated levels of IL-6 in obese compared to non-obese children and adolescents [7-8]. IL-6 contributes to inflammation by raising CRP levels and suppressing adiponectin production. Adiponectin is one of the most abundant adipose tissue–specific cytokines that is closely linked to obesity in both children and adults [9-10]. Serum adiponectin has important anti-inflammatory effect in obesity that inhibits pro-inflammatory cytokines and induces anti-inflammatory cytokines[11]. Unlike other adipocytokines, adiponectin level is decreased in obesity and increased after weight reduction [12-13].

Obesity worsens the severity of asthma symptoms. High BMI and percent of body fat were associated with asthma severity in children [14].

Aim of the present study is to investigate the relation between serum adiponectin level and body composition parameters in obese asthmatic children, its effect on asthma severity.

SUBJECTS AND METHODS

The present study was conducted on 60 children from those attending the Allergy Clinic in Abo El Rich Pediatric Hospital, Faculty of Medicine, Cairo University during the period between 2013 and 2014. Their ages ranged from 7-12 years. The study protocol was approved by the ethical committee of the Institute of Postgraduate Childhood Studies as well as the Medical Ethical Committee of the National Research Centre.

All participants gained comprehensive and clear knowledge about the aim of our work and parental approval and written consents were signed by their parents prior to enrollment.

Cases were divided into 2 groups; group1 comprised 30 non-obese asthmatic children and group 2 comprised 30 obese asthmatic children. Another 30 apparently healthy children of matched age and sex were selected from siblings and relatives of the asthma cases. They were studied as the control group, group 3.

Inclusion criteria include both sexes with age range 7-12 years from diagnosed cases of bronchial asthma either new cases or on treatment with corticosteroids for less than 3 months. BMI <85th percentile were considered non-obese and BMI ≥95th percentile were considered obese children.

Children with any acute disease including upper or lower respiratory tract infections, any chronic disease (heart, liver s, kidney diseases and endocrinal disorders) and cases of asthma on corticosteroid therapy for more than 3 months were excluded from the study.

All cases included in the study were subjected to complete medical history and thorough clinical examination. Severity of asthma was estimated according to the frequency of attacks, nocturnal symptoms, hospitalization, limitation of activity, school absenteeism[15]. Anthropometric measurements in the form of height, weight and body composition parameters (measured by Tanita body composition analyzer), which includes fat mass, fat free mass, percent fat, impedance and total body water. All measurements were made according to techniques described in the anthropometric standardization reference manual [16]. Children were weighed (in kg) using a calibrated Seca scale to the nearest 0.1 kg (Seca, Hamburg, Germany), while height (in cm) was measured using a Seca 225 stadiometer to the nearest 0.1 cm with the children dressed in minimal clothes, and without shoes. Each measurement was taken as the mean of three consecutive readings.

Three milliliters of peripheral venous blood samples were withdrawn under complete aseptic conditions, blood was left to clot at room temperature then centrifuged and sera were separated and stored at -20°C for further evaluations of adiponectin, CRP and IL6.

Serum adiponectin levels were assayed using AviBion Human Adiponectin (Acrp30) ELISA Kit. Cat No: ADIPO25. Serum CRP levels were assayed using BIOS Microwell ELISA diagnostic systems. Ch emux. BioScience. Inc. Cat No: 10110. Serum IL-6 levels were assayed using AviBion Human IL-6 ELISA Kit. Cat No: IL06001.

Statistical Analysis: Data were collected and entered to the Statistical Package for Social Science (IBM SPSS) version 21. Qualitative data were presented as number and percentage. Quantitative data were presented as mean ± standard deviation and the comparison between two independent groups with quantitative data were evaluated using 2-tailed unpaired t-test. Pearson's correlation coefficients were used to evaluate correlations between the data exhibiting parametric distribution. Linear logistic regression analysis was performed to examine the relationship between different parameters. Receiver operating characteristic curve (ROC) was used to assess the best cut off point with the sensitivity. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant at $P<0.05$ and $p<0.005$ was considered of highly significant difference.

RESULTS

Demographic and anthropometric data of the three studied groups are shown in table (1). The obese asthmatic group showed highly statistically significant differences regarding weight, BMI, Fat %, FM, FFM, IMP, TBW compared to non-obese asthmatics and control ($P< 0.005$ both). However, the height showed no statistically significant difference between the two studied asthmatic groups ($P>0.05$). No statistically significant differences were found between non-obese asthmatic cases and the control group as regards the anthropometric data.

Distribution of asthmatic cases according to the severity of asthma is shown in table (2). Non-obese asthmatic cases were classified into 23 mild cases (76.7%) and 7 moderate cases (23.3%). The obese asthmatic cases were classified into 9 mild cases (30%), 18 moderate cases (60%) and 3 severe cases (10%).

The serum levels of the three pro-inflammatory markers of the studied asthmatic cases versus control is shown in table (3). Serum adiponectin level showed highly significant decrease in the obese asthmatics compared to non-obese asthmatics, ($p< 0.005$). On the other hand, serum IL6 and CRP showed highly significant increase in the obese asthmatics compared to non-obese asthmatics, ($p< 0.005$ in both).

Both non-obese and obese asthmatic children showed highly significant increase in serum IL6 and CRP compared to the control group, ($p< 0.005$ in both). However, serum adiponectin level showed highly significant decrease in the obese asthmatics compared to control, ($p< 0.005$).

Correlation between the inflammatory markers and the body composition parameters in obese asthmatic cases is shown in table (4). In obese asthmatics, serum adiponectin showed negative significant correlation with both fat % and impedance ($p<0.05$), and positive significant correlation with FFM ($p<0.05$).

Correlations between the severity of asthma and pro-inflammatory markers in obese asthmatic groups is shown in table (5). Significant negative correlation was found between serum adiponectin level and severity of asthma in obese asthmatics ($r= -0.576$, $p<0.001$).

In order to identify the predictors of asthma severity, linear regression studies were done using the severity of asthma as a dependent factor in obese asthmatic cases. BMI and serum adiponectin level were found to be significant predictors for the severity of asthma in obese asthmatics ($p<0.05$ both), as shown in table (6).

Comparing the ROC sensitivity tests of the three pro-inflammatory markers revealed that adiponectin level is more sensitive test (86.8 %) in detecting the severity of asthma in obese asthmatics compared to serum IL 6 (45.4 %) and CRP (47 %), (figure 1).

DISCUSSION

A linear relationship between asthma severity and BMI was reported in asthmatic cases [17-18]**.** Obese asthmatic patients were found to have worse asthma-related quality of life, worse asthma control, and

more asthma–related hospitalization when compared to asthmatics with normal BMI[19]. Moreover, obese asthmatics were reported 2.5 times more likely to experience dyspnea, have a higher use of inhalers and bronchodilators, and require longer periods of hospitalization compared to non-obese ones independent of age or gender[20-21]. Accurate assessment of body fatness may be important in understanding the relationship between obesity and asthma[22].

In the present study, severe and moderate degrees of asthma were encountered more among obese asthmatic children when compared with non-obese ones. This finding is in concomitant with the conclusion of the American Thoracic Society workshop in 2010 "asthma in the obese may represent a unique phenotype of asthma, with more severe disease that does not respond to conventional therapy" [23].

In contrast to our study, no significant association between severity and duration of asthma with obesity or overweight was found in asthmatic children [24] and in asthmatic adults [25].

Many researches discussed the etiological relationship between obesity and asthma and defined a distinct obesity-asthma phenotype. Many theories have been proposed for this relationship. Firstly, genetic and environmental factors may increase the risk of obesity concurrently with asthma[26-27]. Secondly, obesity may increase the risk of asthma through its effects on other disease process as sleeping-disordered breathing and gastro-esophageal reflux disease[28-29] that are associated with an increased risk for asthma[30-31]. Thirdly, morbid obesity can increase asthma via mechanical mechanisms by reducing lung volume and airway diameter[32-33]. Lastly, obesity is accompanied by increased serum concentrations of adipokines (cytokines, chemokines, acute phase proteins and energy regulating hormones produced by adipocytes) [34-35].

Obese subjects were reported to have significantly higher serum levels of IL-6 and CRP compared with non-obese. Serum levels of IL-6 and CRP were found significantly positively correlated with weight and BMI in obese[6-36]. Several studies have revealed a positive relationship between BMI and CRP with significantly higher CRP levels in obese children and adolescents compared to non-obese children[37].

Significantly low plasma adiponectin level was reported in obese children in comparison to normal-weight for age ones[38]. Plasma adiponectin level was found significantly negatively correlated with BMI[39-40-41]. Moreover, significant negative correlation between adiponectin, BMI & fat mass % with no correlation was found with body weight in obese children[42].

The current study showed highly significant increase in serum IL6 and CRP with highly significant decrease in serum adiponectin level in the obese asthmatic group compared to both non-obese asthmatics and control groups. Serum adiponectin level in obese asthmatics showed negative significant correlation with both fat % and impedance, positive significant correlation with fat free mass but non significant negative correlation with BMI was found.

Our findings are in accordance to other studies conducted on obese asthmatic children where serum adiponectin levels of lean asthmatics were reported significantly higher than those of obese asthmatics[43-,44]. Adiponectin had significant negative correlations with body weight, BMI, and fat %, with significant positive correlations with the fat free mass in obese asthmatic children[44].

On the contrary, some studies showed no statistically significant association between obesity and biomarkers of inflammation in children with asthma[45].

Our study showed that BMI and serum adiponectin level were found to be significant predictors for the severity of asthma in obese asthmatics. Moreover, serum adiponectin level showed a significant negative correlation with the severity of asthma in obese asthmatics.

In favor to the present study, increased body mass index was reported as a predictor for the severity of asthma symptoms in asthmatics[46]. Low serum adiponectin was reported to be more important than body mass index in predicting the risk for incident asthma in premenopausal women[47]. In a retrospective cohort study, an elevated CRP level and BMI z scores were reported to be associated with obesity and asthma severity[48].

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In the present study, comparing the ROC sensitivity tests of the three pro-inflammatory markers revealed that adiponectin level is a more sensitive test (86.8 %) in detecting the severity of asthma in obese asthmatics compared to serum IL 6 and CRP.

Table 1: Demographic and anthropometric data of studied groups

	Obese asthmatics	Non-obese asthmatics	Control
Age in years	9.5 ± 1.6	8.9 ± 1.6	8.8 ± 1.6
Sex: **Male** **Female**	 19 (63.3%) 11 (36.7%)	 20 (66.7 %) 10 (33.3 %)	 11 (36.7%) 19 (63.3%)
Height (cm)	136.5 ± 10.1	133.5 ± 10.1	133.7 ± 10.6
Weight (kg)	57.7* ± 9.1	31.6 ± 8.7	30.5 ± 8.3
BMI(Kg/m^2)	30.8*±0.8	17.4±2.9	16.6±2.0
Fat%	52.5°±77.7	17.5±7.2	17.6±6.2
FM (Kg)	20.8*±6.4	5.9±3.7	5.7±3.1
FFM (Kg)	32.3*±8.7	25.9±6.3	24.8±5.8
IMP (Ω)	501.5*±58.4	606.8±72.1	624.5±72.7
TBW (Kg)	23.7*±6.3	19.0±4.7	18.1±4.3

BMI: body mass index, FM: fat mass, FFM: free fat mass, IMP: impedance, TBW: total body water

Table 2: Distribution of cases according to the severity of asthma

Severity	Non-obese asthmatics		Obese asthmatics	
	No.	%	No.	%
Mild	23	76.7%	9	30%
Moderate	7	23.3%	18	60%
Severe	-	-	3	10%

Table 3: Laboratory findings of the three studied groups

	Non-obese asthmatics	Obese asthmatics	Control
Adiponectin (ng/ml)	18606.7 ± 6610.9	13113.3*$^{\neq}$ ± 4094.5	17300.0± 6162.1
IL6 (pg/ml)	135.9° ± 175.6	886.1*$^{\neq}$ ± 642.9	14.2 ± 14.8
CRP (mg/l)	6.2°± 2.9	11.8*$^{\neq}$ ±2.1	4.2 ± 1.6

*Highly significant statistical difference (p< 0.005) comparing obese asthmatic children with non- obese asthmatic and control group.

$^{\neq}$Highly significant statistical difference (p< 0.005) comparing non- obese asthmatic with control group

°Highly significant statistical difference (p< 0.005) comparing non- obese asthmatic with control group.

Table 4: Correlation between the inflammatory markers and the body composition parameters in obese asthmatic cases

		Weight	BMI	Fat%	Fat mass	FFM	Impedance
Adiponectin	r	-.292	-.260	-.370*	-.106	.423*	-.455*
	p	.118	.165	.044	.577	.020	.011
IL6	r	.042	.103	.062	-.060	-.096	.175
	p	.825	.589	.746	.751	.614	.355
CRP	r	-.052	-.133	-.144	-.213	.066	.013
	p	.785	.483	.447	.258	.728	.947

r: Pearson correlation

P: significance

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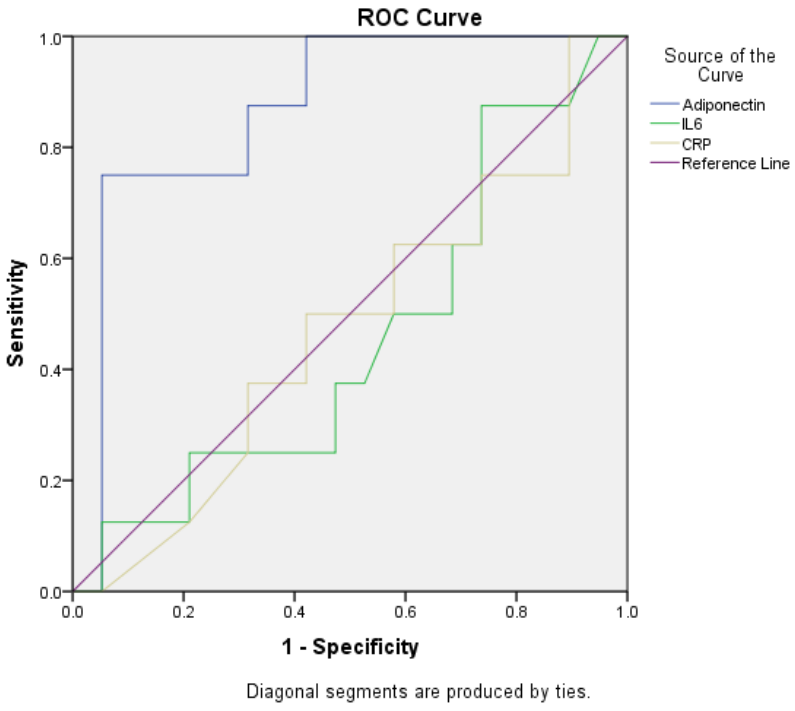
Table 5: Correlation between the severity of asthma and the pro-inflammatory markers in obese asthmatic cases

pro-inflammatory markers		Severity of asthma
Adiponectin	r	-.576
	p	.001
IL 6	r	.123
	p	.516
CRP	r	.018
	p	.924

Table 6: Linear regression for the severity of asthma in obese asthmatic cases

Model	Unstandardized Coefficients	Standardized Coefficients	t	Sig.
	B	Beta		
Adiponectin	-4.231	-.284	-1.720	.010
IL6	.000	.185	1.292	.210
CRP	-.002	-.008	-.056	.956
BMI	.363	.537	2.237	.036
Fat percent	-.053	-.585	-1.784	.089
Fat mass	.029	.303	.892	.382
impedance	-.003	-.267	-1.072	.296
FFM	-.019	-.293	-1.021	.319
a. Dependent Variable: severity of asthma				

Figure 1: Receiver Operator Curve (ROC) of the three pro-inflammatory markers and asthma severity in obese asthmatic children



CONCLUSION

Obesity aggravates the severity of asthma. Adiponectin markedly decreases in obese asthmatic children which plays a role in worsening asthma symptoms. CRP and IL6 increase sharing a big deal in the inflammation process. The negative significant correlation between adiponectin and severity of asthma, points out the important role of adiponectin in the inflammatory process of asthma with or without obesity.

Regular follow up of body composition parameters is recommended in obese asthmatic children beside weight loss interventional programs should be carried out in relevance to the level of adiponectin and severity of asthma symptoms.

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