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Obese Asthmatic Versus Asthmatic Obese Children Regarding: Pulmonary Function Test, Lipid Profile and Serum Eotaxin

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ABSTRACT

Introduction: Obesity and asthma are two common medical conditions that happen to coexist. Their interrelationship is still a matter of debate. Aim: To compare fat distribution, pulmonary function test (PFT), lipid profile and serum eotaxin level in obese asthmatic children and asthmatic obese children. Material and Methods: Twenty eight obese asthmatic children in whom onset of obesity preceded the onset of asthma (group I) and 22 asthmatic obese children in whom asthma preceded the onset of obesity (group II) were included in the study. All children were subjected to clinical and anthropometric evaluation as well as pulmonary function test. The lipid profile (triglyceride, total cholesterol, low-density lipoprotein, and high-density lipoprotein) and serum eotaxin were assessed. Results: This study found a statistically significant increase in triglyceride(TG) and serum eotaxin ($p<0.01$ and 0.003 respectively) in group I . Also, forced vital capacity (FVC), and peak expiratory flow rate (PEFR) showed a statistically significant decrease ($p<0.02$ and 0.01 respectively) in group I. Conclusion: Our data suggest that there are phenotypic differences between both groups. These preliminary results are encouraging to conduct more extensive clinical studies.

Key words: Asthma, eotaxin, lipid, obesity, FVC, PEFR.

Introduction

Asthma and obesity are two chronic inflammatory conditions which are common pediatric problems. Interestingly, during the last 3 decades the incidences of both obesity and asthma have shown a steady increase (Beuther *et al.,* 2006; David *et al.,* 2007). Although it appears to be an interrelation between asthma and obesity; yet, the sequence of their co-existance is still a matter of debate (Elamin, 2004).

Most researchers have presumed that asthma preceded obesity. The common assumption is that weight gain occurs because many asthmatic patients avoid exercise since physical activity can trigger their symptoms (Nick Hacken, 2009). Others suggested that obesity precedes the development of asthma. Proposed mechanisms for the influence of obesity on development of asthma include airway inflammation, mechanical factors, increased airway hyper-responsiveness (AHR), decreased physical activity, and changes in diet (Rachel, 2007). Previous reports suggested that asthma induced obesity may differ phenotypically from asthma in normal-weight individuals. Obesity in the absence of asthma causes physiologic impairments in lung function, including reduction in lung volumes (Biring *et al.,* 1999), chest wall restriction (Naimark & Cherniack 1960) and increased work of breathing(Cournand *et al.,* 1954). In addition obesity contributes to co morbid conditions such as gastro-esophageal reflux (Hampel *et al.,* 2005; Jacobson *et al.,* 2006) and sleep apnea; which can result in dyspnea and wheezing, and might be mistaken for asthma by patients and clinicians(Sin *et al.,* 2002) . Perhaps obesity triggers asthma through hormonally driven inflammation.

Eotaxin, a CC chemokine, has been shown to be a key chemotactic agent responsible for eosinophil-mediated bronchial inflammation in extrinsic or allergic asthma (Ponath *et al.,* 1996). Circulating eotaxin levels in visceral adipose tissue were increased in obesity in mice and humans. Adipose tissue explants secrete eotaxin, and the stromal/vascular component of adipose tissue seems to be the predominant source of eotaxin (Abu R. Vasudevan *et al.,* 2006). This is the first study to compare fat distribution, PFT, lipid profile and serum eotaxin level in obese asthmatic children versus asthmatic obese children.

Subjects and Methods

Twenty eight obese asthmatic children in whom onset of obesity preceded the onset of asthma (group I) and 22 asthmatic obese children in whom asthma preceded the onset of obesity (group II) were included in the study. Group I had age ranged from 7-15 years with mean age 9.38±1.81 years. While group II had age range from 6 -13 with mean age 8.50 ±1.74 years with no statistical variation . Informed consents were taken from the parents of our studied groups according to the guidelines of ethical committee of National Research Centre, Egypt. We recruited asthmatic obese children from Pediatrics outpatient clinic of the National Research Centre during the period between December 2011 till January 2013 . Participants were eligible if they had

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documented physician-diagnosed asthma .Obese asthmatics had body mass index [BMI] ≥ 95th percentile for weight (Neovius & Rasmussen, 2008). Subjects who refused to provide an informed consent, or had secondary obesity such as Cushing syndrome, children with obesity due to corticosteroid therapy or hypothyroidism or children with dysmorphic features suggestive of syndromes (e.g. Laurence –Moon-Biedl or Prader Willi),or received drug therapy which could interfere with the proposed tests were excluded from the study.

All studied children were subjected to the following, full history taking including complete present history with special emphasis on episodes of wheezes, cough, dyspnea, nocturnal symptoms, allergic history, history of medication, and history of other systemic disease. Social history including housing condition and pets, family history, and past history were recorded. Clinical examination, both general and systemic were also performed with special emphasis on weight (Wt) and height (Ht). Calculation of body mass index (BMI) was done by dividing person's weight (Kg) by square height (meters) kg/m²and BMI was further plotted on Egyptian growth curves (Egyptian growth curves, 2009). Waist and hip circumferences were measured according to the World Health Organization criteria: with participants wearing light clothing, waist circumference was measured at the level midway between the lowest rib margin and the iliac crest. Hip circumference was measured at the widest level over the greater trochanters in standing position, waist hip ratio is calculated. Abnormal W/H is considered if >0.86. Measurement of skin folds thickness particularly around triceps, subscapular, and abdominal skin fold thickness were performed (Ismail *et al.,* 2011).

For basal respiratory function test parameters, we measured vital capacity (VC) forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC, and peak expiratory flow rate (PEFR) using Fleisch spirometer. We used % predicted values for comparison between groups.

Laboratory examination

Blood samples:

5 ml of blood were withdrawn from anticubital vein under aseptic precautions from fasting (for 12 -14 hours) subjects. Complete blood picture was done

After centrifugation serum was collected from each subject to evaluate:

1- Lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride) in sera were determined by chemistry analyzer Olympus AU 400.
2- Thyroid hormone (in order to exclude cases of hypothyroidism from the study).
3- Serum Eotaxin level: Using human serum eotaxin kit (LOT 7J12/1) by Invitrogen Corporation (www.invitrogen.com) The Invitrogen Hu Eotaxin kit is a solid phase sandwich Enzyme Linked-Immuno-Sorbent Assay (ELISA) (Abu R. Vasudevan *et al .,* 2006) .

Statistical analysis

Data were statistically described in terms of range, mean ±standard deviation (SD), median, frequencies (number of cases), and percentages when appropriate. . Comparison of quantitative variables between the study groups was done using Mann Whitney U test for independent samples. A probability value (P-value) less than 0.05 was considered statistically significant. All statistical calculations were carried out using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, Illinois, USA) version 15 for Microsoft Windows.

Results:

Table (1) showed a high significant difference (p =0.001) in BMI between group I and group II and a significant difference (p=0.03) in waist circumference between the same groups.However, no significant differences existed between both groups as regards others anthropometric measurements ,triceps skin fold thickness fold thickness (TSFT), subscapular skin fold thickness (SSFT) and abdominal skin fold thickness (ASFT) (p>0.05).

Table1. Comparison between anthropometric measurements in group I and group II.

Item	Group I(no=28) Median(mean±SD)	Group II(no=22) Median(mean±SD)	P-value
BMI(kg/m²)	40(39±6.3)	31.6(31.3±3.7)	0.001
WC(cm)	83.6(82±8.25)	76.5(76.2±6.05)	0.03
HC(cm)	93.7(93±11.9)	86.6(85±0.12)	NS
WHR	0.88(0.8±0.04)	0.88(0.8±0.04)	NS
TSFT(cm)	15.6(14±5.8)	14.2(12.5±3.7)	NS
SSFT(cm)	17.7(16±4.2)	15.9(15±2.7)	NS
ASFT(cm)	21(20.37±35)	18.8(18±3.9)	NS

BMI ,body mass index; WC, waist circumference; HC, hip circumference ;; cm, centimeters; SSFT, subscapular skin fold thickness; TSFT, triceps skin fold thickness; ASFT, abdominal skin fold thickness.

Table (2) showed a significant decreased in FVC and PEFR in group I versus group II. ($p<0.02$ and 0.01) respectively. No significant difference found between the two groups as regard the rest of parameters including FEV1 and FEV1/FVC although they were lower than expected in normal individual.No significant difference ($p>0.05$) was found between both groups as regard hemoglobin concentration, white blood cell count and eosinophil count (Table 3).Our result showed a statistically significant increase in TG level ($p=0.01$) in group I compared to group II . There was no significant difference found between 2 groups regarding other parameters of lipid profile (P value≥0.05). As regards to eotaxin level, a statistically significant increase in group I compared to group II (Table4).

Table 2. Comparison between respiratory function tests in group I and group Π.

Item	Group I(no=28) Median(mean±SD)	Group Π(no=22) Median(mean±SD)	p-value
FVC	61(62.5±9.1)	73(70.9±7.7)	0.02
FEV1	63(62.7±10)	69(69±9.2)	NS
FEV1/FVC (%)	92.9(86.4±17)	98.3(93.5±7.70	NS
PEFR(L/S)	56.2(54.5±11.0)	63(67.6±12.3)	0.01

FVC, forced vital capacity; FEV1, forced expiratory volume in the first second; PEFR, peak expiratory flow rate

Table 3. Comparison between blood picture in group I and group Π.

Item	Group I(no=28) Median(mean±SD)	Group Π(no=22) Median(mean±SD)	p-value
Hb (gm/dl)	10.1(10±1.3)	9.4(9.7±1.1)	NS
WBCs (10/cmm)	13.4(13.2±2.5)	12.2(11.5±2.5)	NS
Eosinophil count (%)	10(9.7±4.4)	10(9.4±4.7)	NS

Hb, hemoglobin; WBCs ,white blood cells

Table 4. Comparison between lipid profile and serum eotaxin in group I and group Π.

Item	Group I(no=28) Median(mean±SD)	Group Π(no=22) Median(mean±SD)	p-value
TG (mg/dl)	136(141.2±12.9)	126(127.7±11.8)	0. 01
Cholesterol (mg/dl)	196.2(194.4±18.8)	195.5(195.5±13.1)	NS
LDL (mg/dl)	168(167.6±13.5)	163(165.8±18.7)	NS
HDL (mg/dl)	48.9(48.9±6.2)	51.5(51.5±9)	NS
LDL/HDL	3.3(3.4±0.6)	3.3(3.3±0.7)	NS
Eotaxin (pg/ml)	394(389.5±72.6)	316.9(312±38.9)	0.003

HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride.

Discussion

To date, studies have not yet explored the differences between asthmatic patients who were obese prior to asthma diagnosis and those who become obese after asthma diagnosis. To the best of our knowledge, this is the first study to explore these differences in Egypt. Our study included 50 asthmatic children divided into two groups according to the onset of obesity group I (patients who started obesity before asthma diagnosis, 28 patients) and group Π (patients started obesity after asthma diagnosis, 22 patients).

We observed a statistically significant increase in body weight and BMI in group I compared to group Π. This is in agreement with Van Gaal *et al.,* 2006 who reported that, with obesity there is an increase in different levels of different cytokines and inflammatory markers which might increase the risk of asthma occurrence. Also Hacken, 2009 reported that there was a relation between obesity, increased risk of asthma development and physical inactivity.

As regards the lipid profile, we observed a statistically significant increase in triglyceride in group I ccompared to group II. With no significant differences in cholesterol, LDL, HDL and LDL/HDL. This is in concordance with McAdams *et al.,* 2007 who reported that obesity has a direct causal link with high levels of triglycerides which are the primary fat in human bodies and the main constituent in energy system. People who are overweight tend to have much higher levels of these fats. Smith *et al.,* 2000 found that triglyceride synthesis has been assumed to occur primarily through acyl CoA: diacylglycerol transferase (Dgat). Dgat has been considered necessary for adipose tissue formation.

As regards the respiratory function both FVC and PEFR were significantly lower in group I (who were with higher weight, BMI and waist circumference) than in group Π suggesting severe small airways obstructive effect. There was no significant difference in FEV1 between groups although its level was lower than normal in both groups. This is in agreement with Biring *et al.,* 1999 who reported that the more the degree of obesity the more the airflow limitation, with reduction of both forced expiratory volume (FEV1) and forced vital capacity (FVC). This reduction in airflow is typically symmetric and results in a preserved FEV1/FVC ratio. Furthermore El-Helaly *et al.,* 2009 reported a decrease in respiratory function parameters in obese children followed by improvement with weight loss. Also, Hammerman *et al.,* 2002 and Hong and Mahmitra 2005 found that obesity lowers all the parameters of respiratory function test (FVC, FEV1, PEFR). As regards to the serum eotaxin level, it was significantly higher in group I compared to group Π. Curat *et al.,* 2004 reported that eotaxin is a

secretory product of adipose tissue and its expression is increased in obesity. Moreover, Ismail *et al.,* 2011 and Kuperman *et al.,* 2002 reported that elevated systemic level of eotaxin derived from adipose tissue contributes to the signs and symptoms of asthma by promoting allergic inflammation in the lung and possibly by directly altering the airways to become more hyper- responsive.

Conclusion

Our data suggest that there are phenotypic differences between asthmatic patients who started obesity before asthma diagnosis and those who started obesity after asthma diagnosis. These preliminary results are encouraging to conduct more extensive clinical studies.

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