The Egyptian Journal of Hospital Medicine (Oct. 2011) Vol., 45: 585 – 594

The Relation between Asthma, Body Fat Distribution and Serum Adiponectin in Obese Egyptian Children.

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Abstract

Childhood obesity is an emerging global public health challenge. That is because the prevalence of obesity among children and adolescents has increased greatly in all parts of the world. A number of studies have reported an inverse relation between respiratory function and various indices of obesity or fat distribution (*El-Baz et al., 2009)*. Adiponectin, an antiinflammatory adipocytokine, circulates at lower levels in the obese, which is thought to contribute to obesity-related inflammatory disease as bronchial asthma *(Medoff et al., 2009)*.

Aim of the work

The aim of this work was to assess the correlation between the bronchial asthma, obesity, fat distribution and serum adiponectin in obese Egyptian children.

Subjects and Methods

The present study included a group of obese fifty (50) children (25 boys & 25 girls) without the co morbidities of the metabolic syndrome; aged 7-18 years, mean age (14.2±3.9). Obesity without the co morbidities of the metabolic syndrome was defined as a BMI above the 85th percentiles according to BMI Charts of Egyptian Growth Charts for boys and girls from 2-21 years (2002). They were compared to thirty (30) lean sex and age matched controls mean age (14.1±4.8) (15 boys & 15 girls) with BMI between the 10th and 75th percentile. Anthropometric measurements (body weight, BMI, WC and fat mass% by DEXA) were done for all children together with pulmonary function test and assessment of serum adiponectin levels.

Results

Weight, Waist circumference (WC), Body mass index (BMI), fat mass% and adiponectin were significant higher in obese compared to non obese groups ($p<0.001$ for all). Parameters of pulmonary function was significant lower in obese compared to non obese groups as regard forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow maximum (PEF) and forced midexpiratory flow 25%(FEF25%) ($p<0.01$ for all). while no significant difference was found between both groups as regard FEV1\FVC ratio and forced midexpiratory flow rate(FEF25-75%)($p>0.05$ for both).

A negative association of BMI with parameters of pulmonary function was found but only FEV1, FVC & FEF 25% were statistically significant($p<0.01$ for all). As regard WC it was negatively correlated with FEV1, FVC and FEF 25 %($p<0.01$ for all) but no correlation was found with other parameters of pulmonary functions ($p>0.05$). In the present study a negative correlation was found between fat mass % and parameters of pulmonary function but none of them was statistically significant ($p>0.05$ for all).

A negative significant correlation was found between adiponectin and age in obese group ($p>0.05$) .As regard anthropometric parameters in obese group a significant negative correlation was found between adiponectin and BMI, WC & fat mass %($p<0.01$ for all) while no correlation was found with body weight($p>0.05$). As regard of pulmonary function parameters a negative significant correlation was found between serum adiponectin and FVC and PEF %($p<0.01$ for both) while a negative correlation was found between adiponectin and FEF 25% but this correlation was statistically insignificant ($p>0.05$), While no correlation was found with FEV1\FVC ratio ($p>0.05$).

Conclusion:

The increasing prevalence of overweight and obesity among Egyptian children may be an important contributor to the increasing incidence and prevalence of asthma. Adiponectin may be one of the signals linking obesity with asthma.

Key words:
Adiponectin, obesity, children, BMI, WC, fat mass%, pulmonary function test.

Introduction

Childhood obesity is an emerging global public health challenge. That is because the prevalence of obesity among children and adolescents has increased greatly in all parts of the world. There is no doubt that the percentages are even greater nowadays because of physical inactivity and westernization in diet *(El-Baz et al., 2009)*. In Egypt, *Salem et al. (2002*) found that the prevalence of obesity among children and adolescent was 14.7% and15.08% for males and females respectively.

Asthma is a common disease in children that forms a major co-morbidity illness *(Zedan et al., 2009)*. Under-diagnosis of childhood asthma represented one of the pitfalls in the asthma management *(Zedan et al., 2009)*. In some communities, the prevalence of asthma among school-age children exceeds 25 percent, and prevalence has been rapidly rising in many regions of the developed world *(Gilliland et al., 2003).Zedan et al., (2003)* found that the prevalence of asthma among school children in Egyptian Delta was 7.7%.

It has long been recognized that obesity is more common among children with asthma, and associations between asthma and high body mass index (BMI) have been observed in cross-sectional studies of adults and children *(Moudgil, 2000)*. These associations have been explained as evidence that asthma causes obesity due to a lack of physical activity among children with asthma *(Gilliland et al., 2003)*.

Adiponectin, the most abundant adipocytokine has a wide range of metabolic, antiinflammation and antiproliferative activities (Okamoto *et al.,* 2006). Of note,
individuals with obesity have low plasma adiponectin levels, suggesting that decreased adiponectin levels may contribute to the increased inflammatory state in obesity *(Medoff et al., 2009)*.

In children and adolescents, the BMI changes markedly with age and differs between boys and girls, and so is most appropriately considered as the 'BMI for age' and interpreted using percentile cut-offs*(Reilly ,2010)*. The use of BMI for age to define being overweight and obesity in children and adolescents is well established for both clinical and public health applications (*Must & Anderson, 2006)*.

Waist circumference is established as a useful method for diagnosing being overweight and obesity in adults, and its use for the same purpose in children and adolescents has been increasing *(Reilly, 2010*).

Dual-energy x ray absorptiometry (DEXA) was introduced as an alternative technique for assessment of total as well as regional body composition in adults and children (Taylor *et al*., 2000*)*.The advantage of DXA are the relatively quick scan time (20 min), minimal radiation dose (< 1 m SV or less than one hundredth of the equivalent radiation exposure of one chest x ray) and the measurement of regional as well as total body composition (*Gran et al., 1996)*.

Aim of the work was to assess the correlation between the bronchial asthma obesity, fat distribution and serum adiponectin in obese Egyptian children.

Subjects and Methods

The present study included a group of obese fifty (50) children (25 boys & 25 girls) without the comorbidities of the metabolic syndrome; aged 7-18 years.

Obesity without the comorbiditiess of the metabolic syndrome was defined as a BMI above the 85th percentiles according to BMI Charts of Egyptian Growth Charts for boys and girls from 2-21 years (2002) (*El-Baz et al., 2009)*.Without elevation of blood pressure for age using National Institutes of Health percentiles, normal fasting glucose (<100 mg\dl), no increase in cholesterol (<200 mg\dl) and normal triglycerides (<150 mg\dl) *(Mauras et al., 2010)*.

They were compared to thirty (30) lean sex and age matched controls (12 boys & 15 girls) with BMI between the 10th and 75th percentile.

All children were considered free from recent upper respiratory tract infections. To avoid illness related elevation of inflammatory markers, subjects were studied only if they have no history recent illness, bone fracture or blood draw. They were instructed not to consume any medication including vitamins, herbal medication, or anti-inflammatory drugs within 10 days of the anticipated blood draw. Half of our subjects were among prepubertal children and half were in late puberty (equal or greater than Tanner IV breast in girls & genitals in boys) with a balanced gender distribution. Menstruating girls must have complete period at least 2 weeks previously.

Method:

Lung function test: All patients underwent spirometric assessment to measure their forced expiratory volume in 1 second (FEV_1) and peak expiratory flow rates (PEFs). Patients were instructed to expire for ≥2 seconds and measurements were only accepted if forced vital capacity was more than FEV_1. The device automatically stored the highest of the three correctly performed PEFs on a microchip, along with the accompanying FEV_1.

All children in the study were subjected to the following:

I. Full history taking with emphasizes on symptoms suggestive of chest diseases e.g. asthmatic attacks in previous year, occasional wheezes, persistent wheezes or cough

2. Thorough clinical examination with emphasis on chest examination.

3. Anthropometric measurements:

Children were weighed wearing light clothes and without shoes on a beam scale to the nearest 0.5kg.Hight was assessed without shoes, the child stands with his heels together stretching upward to full extent, the back is straight as possible. It was taken to the nearest 0.5 cm. Body mass index (BMI): was calculated by dividing weight by high square. Waist circumference: was measured at the narrowest point between the rib cage and iliac crest.

Venous blood sample was collected by direct venipuncture after an overnight fast. The samples were centrifuged, serum a liquated and immediately frozen and maintained at -8ºc for a late analysis of adiponectin. Serum adiponectin levels were determined by a commercial kit using an enzyme-linked immunoassay (Mediagnost, Reutlingen, Germany). The sensitivity of the assay was determined to be <4.7% and inter-assay coefficient of variation was <6.7 %(Galler *et a*l ,2007).The parents of the children gave written informed consent after explanation of the nature of the study.

DXA Scanning

All DEXA measurements were obtained with Lunar DPX-L scanner (Soft ware version 1.32,Lunar Corporation Madison WI).The scanner determines total fat mass in kg and as a percentage of body mass; the latter is calculated as {fat mass\(fat mass +lean tissue mass +bone mineral content)}.

Statistical analysis

Data of tests were analyzed using the arithmetic mean, standard deviation (SD), standard error (SE), unpaired students t- test.

Statistical analysis was performed with SPSS program version 9.

P > 0.05 non significant(N.S)

P< 0.01 significant (Sig.)

P < 0.001higly significant (H.S)

Results

As regard table (1) weight, WC, BMI, fat mass% and adiponectin were significantly higher in obese compared to non obese groups (p<0.001 for all). In table (2) as regard pulmonary function parameters it was significant lower in obese compared to non obese groups as regard FVC, FEV1, PEF and FEF25% (p<0.01 for all).No significant difference was found between both groups as regard FEV1\FVC ratio and FEF25-75% (p>0.05 for both).

Table (3) shows a negative association of BMI with parameters of pulmonary function but only FEV1, FVC & FEF 25% were statistically significant(p<0.01 for all). As regard WC it was negatively correlated with FEV1, FVC and FEF 25 %(p<0.01 for all) but no correlation was found with other parameters of pulmonary functions (p>0.05). In the present study a negative correlation was found between fat mass % and parameters of pulmonary function but none of them was statistically significant (p>0.05 for all).

In table (4) a negative significant correlation was found between adiponectin and age in obese group ($p>0.05$) .As regard anthropometric parameters in obese group a significant negative correlation was found between adiponectin and BMI, WC & fat mass %($p<0.01$ for all) while no correlation was found with body weight($p>0.05$). As regard of pulmonary function parameters a negative significant correlation was found between serum adiponectin and FVC and PEF %($p<0.01$ for both) while a negative correlation was found between adiponectin and FEF 25% but this correlation was statistically insignificant ($p>0.05$), While no correlation was found with FEV1\FVC ratio ($p>0.05$).

Table (1): Comparison between obese and non obese groups as regard age, anthropometric measurements and serum adiponectin levels.

	Obese group n = 50 mean ±SD	Non obese group n = 30 mean ± SD	P value
Age (years)	14.2 ± 3.9	14.1 ± 4.8	>0.05
Weight (kgm)	82 ± 12.8	37.4 ± 13.2	<0.001
WC (cm)	92.0 ± 11.6	70.3 ± 8.1	<0.001
BMI (kg/m²)	35.9 ±6.85	18.8 ± 4.8	<0.001
Fat mass %	38.7 ± 1.7	20.9 ±0.9	<0.001
Adiponectin µg/ml	8.7 ± 0.4	13.4 ± 0.9	<0.001

Table (2) Comparison of pulmonary function parameters between obese and non obese groups

	Obese group n = 50 mean ±SD	Non obese group n = 30 mean ± SD	P value
FEV %	84.38 ± 10.4	96.8 ± 11.3	<0.01
FVC %	85.91 ± 8.2	94.2 ± 10.4	<0.01
FEV_1 / FVC ratio	84.3 ± 12.9	82.4 ± 19.2	>0.05
PEF %	72.5 ± 17.4	80.2 ± 16.1	<0.01
FEF 25%	53.2 ± 12.7	64.9 ± 17.9	<0.01
FEF 25% - 75%	80.9 ± 10.2	92.7 ± 15.9	<0.01

Table (3): Correlation between anthropometric measurements and pulmonary function parameters in obese group.

	BMI (kg/m²)	WC (cm)	Fat mass %

	r	p	r	p	r	p
FEV %	-0.262	<0.01	-0.21	<0.01	-0.020	>0.05
FVC %	-0.256	<0.01	-0.294	<0.01	-0.029	>0.05
FEV_1 / FVC ratio	-0.012	>0.05	0.026	>0.05	-0.030	>0.05
PEF %	-0.024	>0.05	0.025	>0.05	-0.029	>0.05
FEF 25%	-0.002	>0.05	-0.309	<0.01	-0.023	>0.05
FEF 25% - 75%	-0.316	<0.01	0.031	>0.05	-0.031	>0.05

Table (4): Correlation between adiponectin and both the anthropometric measurements and parameters of pulmonary function in obese group.

	Adiponectin	
	r	p
Age(years)	-0.26	<0.01
BMI (kg/m²)	-0.32	>0.05
WC (cm)	-0.291	<0.01
Fat mass %	-0.03	>0.05
FEV %	0.31	<0.01
FVC %	0.26	<0.01
FEV_1 / FVC ratio	0.026	>0.05
PEF %	0.21	<0.01
FEF 25%	-0.021	>0.05
FEF 25% - 75%	0.31	>0.05

Discussion

One of the most important developments in pediatrics in the past 2 decades has been the emerging of a new chronic disease; obesity in children and adolescent. The western life style has led to the supersizing of our diet and the downsizing of our activity, with the results that obesity is now the most common chronic illness in children (*Sakol, 2000*).

There is epidemiological data indicating a causal relationship between obesity and asthma. Several studies suggest that weight loss and weight gain may have an effect on the clinical course of asthma (*Canöz et al., 2008)*.

Adipose tissue is an important source of cytokines and contributes to the inflammatory milieu. Apart from general obesity, visceral adipose tissue is the key factor in the formation of low-grade chronic inflammation in obese individuals (*Canöz et al., 2008*).Adiponectin is an adipokine associated with systemic and inflammatory effect (*Thyagrajan et al., 2010)*.

In the present study as expected as body weight, BMI, and WC were significantly higher in obese compared to non obese groups ($p<0.001$ for all).

Hassan et al., (2011) studied the prevalence of obesity among 3708 Egyptian adolescent´s students (1779 boys & 1929 girls) .They found significant difference between obese and non obese children as regard body weight, BMI, and WC.

As regard fat mass % assessed by DEXA there was highly significant difference between obese and non obese children ($p<0.001$).

Fat mass % is an indicator of peripheral obesity. *Mauras et al*., (2010) found a significant difference between obese and non obese children as regard fat mass %.

In the current study serum adiponectin levels were significantly lower in obese compared to non obese children ($p>0.05$). This result is in according with those found by *Reinehr et al., (2004) and Hassan et al., (2011)*.

It has previously been demonstrated in adults that serum adiponectin levels decrease in obese subjects *(Asayama et al., 2003*).This decrease in serum adiponectin occurs in obese children similar to that in adults.

Adiponectin gene expression in adipose tissue paradoxically decreases despite the increase in tissue mass in obesity. The paradox is at least partly explained by the antagonism of tumor necrosis factor-α (TNF-α) to adiponectin and vice versa. TNF-α, which is over expressed in adipose tissue of obese subjects, reduces the expression of adiponectin in adiposities by suppressing its promoter activity *(Asayama et al.,2003)*.

In the present study the obese group showed significant lower values of FVC, FEV1, PEF and FEF25% when compared to the non obese group($p<0.01$ for all).No significant difference was found between both groups as regard FEV1\FVC ratio and FEF25-75% ($p>0.05$ for both).

Same results were found by *El-Baz et al., (2009)* when they studied pulmonary function in 30 obese compared to 15 lean Egyptian children.

Tantisira and Gold (2006) demonstrated that obesity has been one of the factors cited to be associated with classic extrapulmonary restrictive physiology, with spirometric evidence of decreased FVC, FEV1 and preserved FEV1\FVC ratio.

They found that the mechanism behind this cited restrictive defect has generally been the decreases in pulmonary compliance associated with the accumulation of fat in and around the chest wall, diaphragm and abdomen.

Also cellular hyperplasia, alveolar enlargement and reductions in alveolar surface area relative to lung volume occur in obese children *(Li et al., 2003*).

Nawrocki and Scherer (2004) demonstrated that lower significant PEF and FEF25% in obese children denoting obstruction of small air way and so obese children are at high risk to develop bronchial asthma. The possible explanation may be through the influence of obesity on airway smooth muscle function.

Same results were found by *Eisenmann et al.*, (2007) who found statistically significant increase in pulmonary function in normal weight children compared to obese children.

In contrast to our results *Li et al., (2003)* studied the effect of obesity on pulmonary function in obese chiness children. They concluded that obesity doesn't affect spirometric values. This disagreement could be due to the difference in the nature of the study as they did not include a control group, also racial factors may play a role.

In the current study we examined the correlation between the degree of obesity and fat distribution with pulmonary function parameters in obese group. Over all, there was negative association of BMI with parameters of pulmonary function but only FEV1, FVC & FEF 25% were statistically significant.

The effect of BMI on pulmonary function has been evaluated in several pediatric cohorts. El-Baz et al. (2009) found a significant negative correlation between BMI and FEV1, FVC, PEF & FEF 25% while FEV1\FVC ratio and FEF25-75% were not significantly correlated with increased. *Tantisira et al., (2003*) study 1041 childhood asthmatics and found that BMI was positively associated with increased FEV1and FVC. However, increased BMI was corresponding to decrement in the FEV1\FVC ratio. But in our study no significant correlation was found between BMI and FEV1\FVC ratio. They suggested that dover the range of normal to mild obesity BMI is a proxy for growth leading to the association of increase in spirometric volume with increased BMI (*Tantisira et al., 2003*).

As regard WC it was negatively correlated with FEV1, FVC and FEF 25% but no correlation was found with FEV1\FVC ratio, PEF & FEF25-75% was found.

Same results were found by *Chen et al., (2002)* they explained that by the effect of abdominal adiposity on the diaphragm, causing limitation of its free movement. Also *Balcom et al., (2006)* demonstrated that abdominal adiposity is a better predictor of pulmonary function than weight and BMI. Our results are disagreed with *El-Baz et al., (2009*) who found no correlation between WC and all parameters of pulmonary function.

In the present study a negative correlation was found between fat mass % and parameters of pulmonary function but none of them was statistically significant.

These results were disagreed with *Tantisira and Gold (2006)* who found negative significant correlation between fat mass% as an indicator of truncal obesity and parameters of pulmonary function.

In the current study a negative significant correlation was found between adiponectin and age in obese group.

Same results were demonstrated by *Butte et al., (2005*) who found that this decline may be associated with changes in sex hormone and growth factor occurs with age in children and adolescents. As regard anthropometric parameters in obese group a significant negative correlation was found between adiponectin and BMI, WC & fat mass % while no correlation was found with body weight.

The present results were at variance with several publications showing inverse relationship between plasma adiponectin concentration and adiposity and anthropometric measurements (*Hassan et al., 2011, Chu et al., 2005 and Tsou et al., 2004)*.

This goes in concordance with that of *Lee et al., (2006*) who did not demonstrate any correlation between plasma adiponectin and BMI. Also *Schoppen et al.,* (2010) demonstrated that adiponectin was weakly related to BMI, WC and was not correlated with fat mass%. This finding can be attributable to ethnic difference and small samples.

In the present study adiponectin was significantly negatively correlated with WC while no correlation was found with both BMI and fat mass%. Same results were found by *Motoshima et al (2002*).

Waist circumference(WC) is a good indicator for visceral obesity. *Asayama et al., (2003)* reported that cultured human omental adipocytes secreted more adiponectin than subcutaneous adipocytes and that the secretion of adiponectin from subcutaneous tissue was unrelated to BMI.

On the other hand *Reinehr et al., (2004*) found a negative correlation between adiponectin and both BMI and WC.

As regard of pulmonary function parameters a negative significant correlation was found between serum adiponectin and FVC and PEF while a negative correlation was found between adiponectin and FEF 25% but this correlation was statistically insignificant while no correlation was found with FEV1\FVC ratio.

Same results were found by *Thyagarajan et al., (2010*) they demonstrated that adiponectin inhibits pro-inflammatory cytokines such as TNF-α and interleukin 6 (IL-6) and induce anti inflammatory cytokines as IL-10 and IL-1 receptor antagonist. A decrease of adiponectin levels which occurs with obesity leads to increased expression of TNF-α in alveolar macrophages and alveolar simplification and or enlargement. They also suggested that systemic adiponectin, independent of obesity, may have a protective effect on the lung through inhibition of alveolar macrophage related inflammation.

Conclusion

The increasing prevalence of overweight and obesity among Egyptian children may be an important contributor to the increasing incidence and prevalence of asthma. Adiponectin may be one of the signals linking obesity with asthma.

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العلاقة بين الربو و توزيع الدهون بالجسم و ومستوي الاديبونيكتين في الأطفال المصريين الذين يعانون من السمنة

دينا محمد أباظة, أمانى عزالعرب , أنصاف خليل محمد وهدى عز العرب
الغدد الصماء والايض . قسم الصدر والدرن . قسم الاطفال جامعة الأزهر وقسم البكتريولوجى جامعة عين شمس

انتشار البدانة بين الأطفال والمراهقين ازداد الى حد كبير في جميع أنحاء العالم. وأفاد عدد من الدراسات وجود علاقة عكسية بين وظيفة الجهاز التنفسي ومؤشرات مختلفة من السمنة أو توزيع الدهون.
الاديبونيكتين، وهومادة مضادة للالتهاب، توزع على المستويات الأدنى في السمنة، والتي يعتقد أنها تساهم في مرض التهاب الربو القصبي ذات الصلة بمرض السمنة

أهداف البحث
الهدف من هذا العمل هو تقييم الارتباط بين الربو القصبي، والسمنة، وتوزيع الدهون ومستوى مادة الاديبونيكتين فى مصل الدم في الأطفال المصريين الذين يعانون من السمنة.

طريقة البحث

شملت هذه الدراسة مجموعة الأطفال الذين يعانون من السمنة بدون خصائص متلازمة التمثيل الغذائي، الذين تتراوح أعمارهم بين 7-18 سنة، ومتوسط أعمارهم (14.2 ± 3.9). وقد تم تعريف سمنة مرضية بدون خصائص متلازمة التمثيل الغذائي ومؤشر كتلة الجسم فوق 85 % وفقا لمخططات مؤشر كتلة الجسم من مخططات النمو المصري للفتيان والفتيات من 2-21 سنة (2002). وجرى مقارنتهم بثلاثين طفل فى نفس الجنس والعمر- متوسط العمر (14.1 ± 4.8) مع مؤشر كتلة الجسم بين 10 و 75%. وقد أجريت القياسات البشرية (وزن الجسم، ومؤشر كتلة الجسم٪ من الدهون الشامل) لجميع الأطفال مع اختبار وظائف الرئة وتقييم مستويات اديبونيكتين المصل.

و كانت النتائج كالاتى

وكان الوزن، مؤشر كتلة الجسم٪, كتلة الدهون واديبونيكتين كبيرة في البدانة بالمقارنة مع المجموعات غير البدناء (P <0.001 للجميع). وكانت وظائف الرئة منخفضةانخفاض ملحوظ في البدناء بالمقارنة مع المجموعات غير البدناء
تم العثور على وجود ارتباط سلبي من مؤشر كتلة الجسم مع وظائف الرئة وكانت ذات دلالة إحصائية ولكن لم يتم العثور على ارتباط مع غيرها من معالم وظائف الرئة . في هذه الدراسة تم العثور على وجود علاقة سلبية بين كتلة الدهون ٪ ووظائف الرئة. كذلك وجود علاقة سلبية كبيرة بين مستوى الاديبونيكتين والسن في الذين يعانون من السمنة المفرطة. في المجموعة البدينة وجد أن هناك ارتباط سلبي بين مؤشر كتلة الجسم و مستوى الاديبونيكتين و من الدهون الشاملة ٪ في حين لم يتم العثور على أي ارتباط مع وزن الجسم. كما الصددفى وظائف الرئة وجدت علاقة سلبية كبيرة بين مستوى الاديبونيكتين فى المصل و وظائف الرئة

الخلاصة:

تزايد انتشار زيادة الوزن والبدانة بين الأطفال المصريين قد يكون مساهما هاما في تزايد وانتشار الربو.مستوى الاديبونيكتين قد يكون واحدة من الاشارات التي تربط بين البدانة ومرض الربو.