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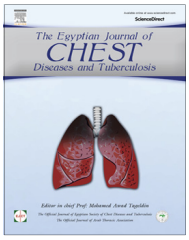

ORIGINAL ARTICLE

Leptin and adiponectin are valuable serum markers explaining obesity/bronchial asthma interrelationship

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KEYWORDS

Bronchial asthma;
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Abstract *Background:* Asthma in the obese represents a growing epidemic of pulmonary disease, and these patients are distinct from non obese asthmatics. Accordingly, studies on the pathogenesis of asthma in the obese are critical to guide our understanding of this disease process; such studies will ultimately guide the development of new therapies to treat the obese asthmatic population.

Patients and methods: Eighty (80) subjects were classified according to BMI into 4 groups: Group 1 (20 subjects): control none obese, they were apparently healthy subjects with BMI 22.9 ± 0.68 kg/m^2. Group 2 (20 subjects): control obese, they were apparently healthy subjects with BMI 36.16 ± 3.15 kg/m^2. Group 3 (20 patients): they were none obese asthmatic patients with BMI 22.97 ± 1.13 kg/m^2. Group 4 (20 patients): they were obese asthmatic patients with BMI 34.9 ± 2.4 kg/m^2.

Results: There was a higher leptin serum level in obese control (34.81 ± 2.32 pg/ml) compared to none obese control (9.73 ± 0.78 pg/ml) ($p < 0.01$). Moreover, there was a higher leptin serum level in obese asthmatic patients (39.74 ± 3.26 pg/ml) compared to none obese asthmatic patients (23.58 ± 1.99 pg/ml) ($P < 0.01$). There was a lower adiponectin serum level in obese control (4.95 ± 1.32) than non obese control (7.74 ± 3.13) ($P < 0.05$) and in obese asthmatic patients (3.3 ± 1.4) than non obese asthmatic patients (5.99 ± 1.5) ($P < 0.01$).

Conclusion: There is a strong association between asthma and obesity regarding serum level of leptin and adiponectin.

Introduction

There is a worldwide epidemic of obesity. In the USA, the prevalence of obesity, defined as a body mass index (BMI) $\geqslant 30$ kg/m^{-2}, has increased among adults aged 20–74 years from, 15% in the late 1970 to, 35% in 2010. The obesity epidemic has impacted both developed and developing nations

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throughout the world. The World Health Organization estimates that worldwide, 2 billion people are either obese or overweight [1]. Not only is obesity a risk factor for asthma, but asthma in the obese has distinct features compared to disease in the non-obese. Obese asthmatics tend to have more severe disease [2,3] respond less well to standard controller therapy, [4] and have evidence of cellular glucocorticoid resistance [5]. This despite the fact they do not appear to have worsened airway inflammation as measured by either sputum eosinophils or neutrophils [6]. Asthma is associated with airway inflammation and reversible airflow obstruction. Obese asthma patients have more severe disease with increased asthma exacerbations, decreased asthma control, and decreased steroid responsiveness [7].

Asthma in the obese represents a growing epidemic of pulmonary disease, and these patients are distinct from non obese asthmatics. Accordingly, studies on the pathogenesis of asthma in the obese are critical to guide our understanding of this disease process; such studies will ultimately guide the development of new therapies to treat the obese asthmatic population [8].

Patients and methods

This study was carried out at Chest Department, Outpatient Clinics at Zagazig university hospitals from April 2013 to October 2013.

Study design: Prospective case control comparative study.

Type of selection: none randomized.

Subjects

The study included 80 subjects who were classified into 4 groups according to BMI and GINA 2012 [9]. Group 1 (20 subjects): control none obese, they were apparently healthy subjects. Group 2 (20 subjects): control obese, they were apparently healthy subjects. Group 3 (20 patients): they were none obese asthmatic patients. Group 4 (20 patients): they were obese asthmatic patients. All Asthmatic persons were diagnosed according to (GINA. 2012) [9].

Inclusion criteria

(1) Asthmatic patients either males or females, non-smokers or ex-smokers for at least 3 months well controlled on inhaled corticosteroids (ICS) with or without long acting β 2 agonist (LABA) [9]. (2) Obese BMI $\geqslant$ 30.3) Non obese have BMI (24.9–20) [10].

Exclusion criteria

Individuals with one or more of the following: known infectious disease, cardiovascular, rheumatic, malignancy, liver and kidney disorders, breast-feeding and pregnant women, and individuals with obesity due to secondary factors were excluded from the study [11]. Bronchial asthma patients who were receiving systemic steroids in the preceding 4 weeks were also excluded. [12].

Methods

All persons were subjected to:

(1) Full medical history: Including history of asthma symptoms especially; breathlessness, chest tightness, wheezing and cough, family history of asthma or atopic diseases, co-morbid disorders eg, DM, HTN, heart failure, liver cell failure and renal failure. (2) Full clinical examination (general examination and local chest examination): 1 – Weight which was measured in kgm, height which was measured in meters and accordingly BMI was calculated. (3) Plain chest X-ray: (postero-anterior view and lateral view) and HRCT chest if needed. (4) Full conventional laboratory investigation eg, CBC, ESR, RBS, liver function tests. (5) Spirometric ventilatory function was done by (Minispir S/N C00215): FEV1/FVC ratio <0.75–0.8 suggests airflow limitation. The degree of reversibility in FEV1 which indicates a diagnosis of asthma is generally accepted as 12% and 200 ml from the pre-bronchodilator value 15 min after inhalation of 200 μg of salbutamol [9]. (6) Measurement of inflammatory markers serum level: Fasting venous blood samples were collected at 09.00 h. After centrifuging at 4 °C, the blood was stored at −70 °C until analyzed [11]:

(A) Leptin: measurement of leptin serum level was done for all cases and control group by ELISA ''Enzyme – linked immunosorbent assay technique''. By (Bio-Rad, Hercules, CA, USA) in accordance with the manufacturer's guidelines. The minimum measurable level of leptin is 7.8 pg/ml.

(B) Adiponectin: measurement of adiponectin serum level was done for all cases and control group by ELISA ''Enzyme – linked immunosorbent assay technique''. 'ELISA KIT' by (anti Biotech OY, Orgenium Laboratories Business Unit, Finland).

Statistical analysis

Statistical analysis was performed with Epi Info™ version 7 and the SPSS version 19 statistical software package (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± SD. For time point differences, a two-sample t test was used. P value <0.05 was considered significant.

Results

Demographic data of the studied population are demonstrated in Table 1 where, group 1 includes 20 subjects (10 males and 10 females) with mean age 33.4 ± 7.6 years, group 2 includes 20 subjects (11 males and 9 females) with mean age 33.6 ± 9.6 years, group 3 includes 20 asthmatic patients (11 males and 9 females) with mean age 31.9 ± 6.2 years, group 4 includes 20 obese asthmatic patients (9 males and 11 females with mean age 34.7 ± 8.08 with $P > 0.05$.

Table 2 shows the mean value of BMI in the studied population with highly statistical differences between group 1 with BMI 22.9 ± 0.68 kg/m^2, and group 2 with BMI 36.16 ± 3.15 kg/m^2, and between group 3 with BMI

Table 1 Demographic data of the studied population.

		Group 1 Non obese control	Group 2 Obese control	Group 3 Non obese asthmatics	Group 4 Obese asthmatics		*P* value
Age	(mean ± SD)	33.4 ± 7.6	33.6 ± 9.6	31.9 ± 6.2	34.7 ± 8.08	*t*-Test	>0.05
Sex						Chi-square	>0.05
Male	*N*	10	11	11	9		
	%	(50)	(55)	(55)	(45)		
Female	*N*	10	9	9	11		
	%	(50)	(45)	(45)	(55)		

Table 2 BMI of the studied population.

	Group 1 None obese control	Group 2 Obese control		*P* value	Group 3 None obese asthmatics	Group 4 Obese asthmatics		*P* value
	(Mean ± SD)	(Mean ± SD)			(Mean ± SD)	(Mean ± SD)		
BMI	22.9 ± 0.68	36.16 ± 3.15	*t*-Test	<0.05	22.97 ± 1.13	34.9 ± 2.4	*t*-Test	<0.05

BMI: body mass index (kg/m^2).

Table 3 Level of control of asthmatic patients.

	Group 3 (20 patient) None obese asthmatics		Group 4 (20 patient) Obese asthmatics	
Day time symptoms	*N*	%	*N*	%
None	12	60	8	40
Once/w	4	20	4	20
Twice/w	4	20	8	40
Need for reliever				
None	12	60	8	40
Once/w	4	20	4	20
Twice/w	4	20	8	40
Limitation of activities	0			0
Night symptoms/ awakening	0	0	0	0
FEV1	92.6 ± 3.8		92.2 ± 3.6	
PEF	81.8 ± 1.32		81.1 ± 1.37	
Controlled	100%		100%	

FEV1: forced expiratory volume in 1 second, PFE: peak expiratory flow.

22.97 ± 1.13 kg/m^2, and group 4 with BMI 34.9 ± 2.4 kg/m^2, with $P < 0.05$.

Table 3 compares between group 3 and group 4 as regards parameters of the level of asthma control. In none obese asthmatic patients (group 3) 60% of patients experienced no day time symptoms nor need for reliever while 20% was in need for reliever once/week and the last 20% experienced day time symptoms and the subsequent use of rescue medication. On the other side, in obese asthmatic patients (group 4) 40% experienced no daytime symptoms nor need for reliever while 20% experienced day time symptoms once/week and was in need for reliever medication once/week, the last 40% experienced day time symptoms and subsequent use of rescue medication twice/week. Both groups gave no history of limitation of activity or night symptoms/awakening with FEV1 and PEF >80% in the last 4 weeks.

Table 4 demonstrates the mean value of FEV1 and PEF in the studied population. There was a lower FEV1 and PEF of obese groups than none obese groups, however there was no significant statistical difference as regards FEV1 and PEF among none obese controls (96.95 ± 3.35, 82.8 ± 2.2) compared to obese controls (94.7 ± 4.5, 82.2 ± 3.1) and none-obese asthmatics (92.55 ± 3.8, 81.8 ± 1.32) compared to obese asthmatics (92.2 ± 3.6, 81.1 ± 1.37), respectively.

In Table 5 there was a higher serum leptin level in obese control (34.81 ± 2.32 pg/ml) compared to none obese control (9.73 ± 0.78 pg/ml) with $P < 0.05$. Moreover, there was a higher leptin serum level in obese asthmatic patients (39.74 ± 3.26 pg/ml) compared to none obese asthmatic patients (23.58 ± 1.99 pg/ml), with $P < 0.01$. There was a lower adiponectin serum level in obese control (4.95 ± 1.32) than non obese control (7.74 ± 3.13) and in obese asthmatic patients (3.3 ± 1.4) than non obese asthmatic patients (5.99 ± 1.5) with $P < 0.01$.

Table 6 and Fig. 1 demonstrate the positive correlation between leptin serum level and BMI where ($r = 0.87$ and $P < 0.01$).

On the other hand Table 7 and Fig. 2: demonstrates the negative correlation between adiponectin serum level and BMI where ($r = -0.6$ and $P < 0.01$).

Discussion

Whether activity restriction causes obesity or obesity by itself causes the development of asthma has been questioned. The possibility that asthma may lead to obesity is less controversial, because of fear of exercise or inability to exercise regularly [13]. Adipose tissue is an important source of cytokines and contributes to the inflammatory state. Apart from general obesity, visceral adipose tissue is the key factor in the formation of low-grade chronic inflammation in obese individuals [14]. More than 50 different adipokines are secreted by adipocytes. Adipokines are proteins that help regulate various body

Table 4 Spirometric pulmonary function of the studied population.

	Group 1 None obese control	Group 2 Obese control		*P* value	Group 3 None obese asthmatics	Group 4 Obese asthmatics		*P* value
	Mean ± SD	Mean ± SD			Mean ± SD	Mean ± SD		
FEV1	96.95 ± 3.35	94.7 ± 4.5	*t*-Test	>0.05	92.55 ± 3.8	92.2 ± 3.6	*t*-Test	>0.05
PEF	82.8 ± 2.2	82.2 ± 3.1		>0.05	81.8 ± 1.32	81.1 ± 1.37		>0.05

FEV1: forced expiratory volume in 1 second, PFE: peak expiratory flow.

Table 5 Comparison between leptin and adiponectin serum levels measured for the studied population.

	Group 1 None obese control	Group 2 Obese control		*P* value	Group 3 None obese asthmatics	Group 4 Obese asthmatics		*P* value
	(Mean ± SD)	(Mean ± SD)			(Mean ± SD)	(Mean ± SD)		
Leptin	9.73 ± 0.78	34.81 ± 2.32	*t*-Test	<0.01	23.58 ± 1.99	39.74 ± 3.26	*t*-Test	<0.01
Adiponectin	7.74 ± 3.13	4.95 ± 1.32		<0.05	5.99 ± 1.5	3.3 ± 1.4		<0.01

Leptin serum level: pg/l, Adiponectin serum level: ng/l.

Table 6 Correlation between leptin serum level and BMI.

	r	*P*
Leptin serum level and BMI	0.87	<0.01

BMI: body mass index (kg/m^2).

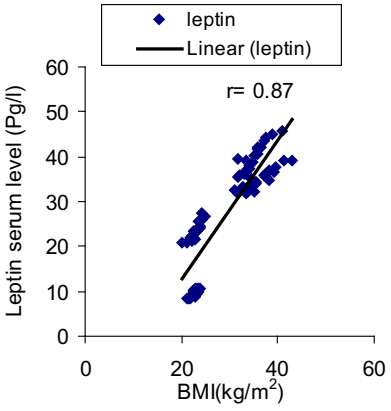

Figure 1 Correlation between leptin serum level and BMI.

Table 7 Correlation between adiponectin serum level and BMI.

	r	*P*
Adiponectin serum level and BMI	−0.6	<0.01

BMI: body mass index (kg/m^2).

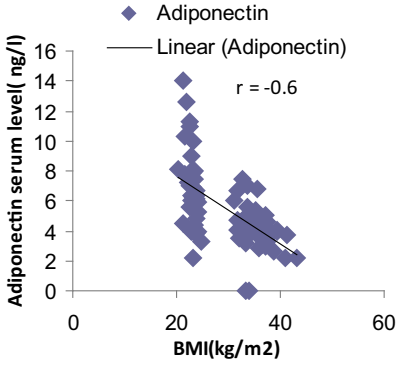

Figure 2 Correlation between adiponectin serum level and BMI.

functions [15]. Leptin and adiponectin are two adipokines that are being studied to determine their association with asthma [16]. There has been intense interest in the potential role of adipose tissue in the development of asthma in obesity. Adipose tissue is an active endocrine organ elaborating cytokines and hormones that regulate metabolism and immune responses. In the lean state, adipose tissue typically secretes low levels of proinflammatory cytokines (e.g., IL-6, IL-8, tumor necrosis factor [TNFα]) and adipokines (e.g., leptin), and produces high levels of the anti-inflammatory adipokine adiponectin. In the obese state, adipose tissue hypertrophies and becomes infiltrated with proinflammatory macrophages. These activated macrophages and hypertrophic adipocytes produce increased proinflammatory cytokines and adipokines, and decreased adiponectin; this "metabolic inflammation" is thought to produce the systemic complications of obesity, such as type 2 diabetes, steatohepatitis, and the metabolic syndrome [17]. Hence this study was done to confirm the interrelationship of leptin and adiponectin serum levels with asthma and obesity.

All asthmatic patients included in this study were in a controlled state according to GINA, 2012 [9] and this is in agreement with Canoz et al. [11] and Scott et al. [12] who selected

their asthmatic patients in a controlled state. Furthermore, spirometric pulmonary function of the studied population showed a lower FEV1 and PEF of obese groups than none obese groups without significant statistical difference; FEV1 and PEF between none obese control (group 1) compared to obese controls (group 2) and none obese asthmatics (group 3) compared to obese asthmatics (group 4) and this is to confirm stability and group matching so the level of inflammatory markers is independent to other modifying factors as one in the study of Canoz et al. [11].

Our study showed a higher leptin serum level in obese asthmatics compared to none obese asthmatics and in obese control compared to none obese control and there was a highly significant statistical association between BMI and leptin serum level with a positive correlation between BMI and leptin serum level. This is in harmony with Scott et al. [12], Abdul Wahab et al. [13], Nirav et al. [18], Bastard et al. [19], Sood et al. [20] who found, especially in women, support for an association of asthma with both serum leptin level and BMI but after adjustment only the association with BMI remained significant, as of McLachian et al. [21] and Claude and Cheryl [22]. However, the study of Jartti et al. [23] documented that increase in BMI was also associated with incident asthma during adulthood but serum levels of leptin, adiponectin or any other obesity-related biomarker were not independently associated with asthma. Adiponectin is one of the most abundant gene products in adipose tissue. In contrast to many of the other adipokines, the levels of which rise in obesity, plasma adiponectin levels are decreased in obesity, and levels increase following weight loss Kern et al. [24]. The study by Sood et al., [25] represented the first step in understanding the role of adiponectin in humans with asthma. Our study showed that serum adiponectin levels were significantly lower among obese asthmatics compared to non obese asthmatics and negatively correlated with BMI and this is in agreement with one study each of children and adults showing a protective association between serum adiponectin concentrations and risk for asthma, but was independent of BMI which was done by Sood et al. [26] and Nagel et al. [27]. However, Abdul Wahab et al. [13] found serum adiponectin is lower in obese asthmatics than none obese asthmatics in their studied population with a highly significant statistical association between BMI and adiponectin. As mentioned above, Jartti et al. [23] did not find an association between adiponectin and asthma.

Conflict of interest

We have no conflict of interest to declare.

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