Leptin, Obesity and IgE in patients with Asthma and Allergic Rhinitis

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Abstract

Background: Asthma is a chronic inflammatory disease of the respiratory airways with a worldwide prevalence. This study was performed to evaluate the role of leptin on asthma and /or allergic rhinitis, and to study asthma-obesity-leptin relationship.

Methods: A cross sectional study was performed on asthmatic patients (190), allergic rhinitis patients (110) and healthy control subjects (48).

Results: Serum leptin was significantly higher at asthma with overweight, asthma with metabolic syndrome, allergic rhinitis with overweight patients than of control subjects, while it was of no significant statistical difference at asthma with normal weight, allergic rhinitis with normal weight patients than of healthy control individuals. Body mass index was significantly higher in asthma with overweight patients; asthma with metabolic syndrome and allergic rhinitis with overweight. It was of no significant difference in asthmatic with normal weight patients, allergic rhinitis with normal weight than of control subjects. FEV1 was significantly lower in asthma with normal weight patientss; asthma with overweight; asthma with metabolic syndrome; allergic rhinitis with normal weight; allergic rhinitis with over weight than in control subjects.

Conclusion: Leptin was significantly higher in patients with asthma and allergic rhinitis as compared to healthy non allergic individuals and it was influenced by BMI and presence of metabolic syndrome in allergic patients. BMI influence FEV 1 in both asthmatic and allergic rhinitis patients.

Key words: Asthma, Allergic rhinitis, Obesity, Leptin, IgE, Metabolic syndrome, BMI.

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Introduction

Obesity is increasing worldwide at an alarming rate in both developed and developing countries, with a global morbidity and mortality impact [1]. Asthma and Obesity have an enormous impact on public health. It has been estimated that up to 65% of adult population of the United States is obese or overweight [2], whilst in Spain about 15% of the population is obese and 39% is overweight, and these figures have increased progressively in recent years. Although bronchial asthma affects a smaller percentage of people, its prevalence has also increased since the 1960s. according to the Centers for Disease Control and Prevention [3].

Both asthma and allergic diseases are associated with a western lifestyle and their prevalence has increased in developed countries [3]. The factors in western lifestyles that have been considered responsible for this increased prevalence are greater exposure to allergens in the home and

changes in contact with different microorganisms [4].

In recent years, many studies in developed countries have suggested a relationship between asthma and factors such as changes in diet and obesity. Although the exact nature of this association has not been fully elucidated, epidemiological data have led researchers to suggest that obesity precedes asthma, increases both its prevalence and severity, and may lessen the efficacy of those drugs normally used in its treatment [5].

Asthma and obesity have a considerable impact on public health and their prevalence has increased in recent years. Numerous studies have linked these disorders. Most prospective studies show that obesity is a risk factor for asthma and have found a positive correlation between baseline body mass index and the subsequent development of asthma. Furthermore, several studies suggest that whereas weight gain increases the risk of asthma, weight loss improves the course of the illness [5].

Materials and Methods

Study Design:

For the present study, a case-control design was used. The cases which were two groups (asthmatic group and allergic rhinitis group) and control group which includes normal persons who are non-asthmatic and non-allergic rhinitis persons (non-atopic).

Study Population:

The study was performed on asthmatic, allergic rhinitis patients and non asthmatic non allergic control subjects. A total of 348 persons included in the study, and their age range was 16 to 60 years. Their subgroups are shown in table 1. The subjects included in the study were outpatients for asthma and allergy units in Baquba Teaching Hospital consultation clinic at the period from 10/9/2010 to 10/5/2012. The diagnosis of asthma and allergic rhinitis was performed by specialists physicians and was established according to American Thoracic Society Criteria [6]. Normal volunteers were also involved in the study as healthy control. (Table1). None of them had any previous history of lung or allergic disease and were not using any medications. They had (most of them) normal lung function test (FEV_1 >80%) and negative skin allergy test.

Asthmatic patients were classified into asthmatic with normal weight, asthmatic with overweight and asthmatic with metabolic syndrome. Allergic rhinitis patients are classified into allergic rhinitis with normal weight and allergic rhinitis with overweight.

Data Collection:

For this study questionnaire interviews and face to face interviews were used to collect data from individuals (case and control groups).

Blood Sampling and Processing:

Twelve hours fast blood samples were collected from the cases and controls by well trained and experienced technicion. About 6.0 ml of venous blood was drawn from each individual. The serum samples were rapidly separated by centrifugation for 10 minute at room temperature at 3500 rpm. The separated serum was divided into two plastic tubes, one stored at 2-5°C for no more than 24 hours prior lipid profile determination, and the second one was frozen at -70°C for serum human leptin and human total IgE.

Determination of Leptin:

Serum leptin determined using DRG-USA- Germany Kit. The detection procedure was performed according to manufacturer instructions.

Determination of IgE:

IgE serum level determined using DRG-USA- Germany kit. The procedure was performed according to manufacturer instructions.

Measurement of BMI

The body weight of each individual dressed in light clothing without shoes using a carefully calibrated electrical balance (*e-Accura*), the height of each individual was measured using vertical measuring rod. BMI was calculated as weight (kg) divided by squared height (m^2).

Data Analysis

Data were analyzed using Statistical Package of Social Sciences (SPSS) system (version 13.0).

Results

Our study population is composed of 348 individuals; 300 individuals are case groups and 48 individual is control group. The mean age of the patients included in the study was 34.34 ± 11.58 years, the mean age for male was 32.21 ± 12.58 years and for female was 37.26 ±8.72 years.

Distribution of study population by gender.

A total of 348 individuals are included in this study from them 136 (39%) individuals were males and 212 (61%) individuals were females; this distribution is shown in Table 1.

Distribution of the Study Population by Age:

Table 2 shows that 28.73% of individuals among the case and control groups were between the age of 31-40 years, 23.56% between the age of 21-30 years, 17.24% between the age of 16-20 years and the age of 41-50 years and 13.21% between the age of 51-60 years.

Serum Leptin:

In this study serum Leptin was found higher in asthma with overweight, asthma with metabolic syndrome and allergic rhinitis with overweight groups than in control group, mean were 12.97± 5.095 ng/ml, 17.096± 9.271 ng/ml, 13.783± 4.929 ng/ml and 4.31±3.8 ng/ml and P-value was <0.0001 which was of extreme statistical significance. Serum Leptin in asthma with normal weight and allergic rhinitis with normal weight is not of significant statistical difference than of control group; mean were 4.88±2.61 ng/ml, 4.374± 1.626 ng/ml and P-value were 0.1789, 0.936 (table 3).

In studying serum Leptin according to the gender it was also found higher at the groups asthma with overweight, asthma with metabolic syndrome than in control group; means were 8.93 ± 3.76ng/ml (male),14.76±4.52 ng/ml(female); 12.53±4.61 ng/ml(male),18.35±9.856 ng/ml(female) and for control group it was 4.18±1.59 ng/ml (male), 4.34±1.84 ng/ml(female). P-value was of extreme statistically significant difference in these groups and it was 0.001. while study of serum Leptin in asthma with normal weight, allergic rhinitis with normal weight groups it was not of statistical significant difference than in control group and mean was 4.75±3.03 ng/ml (male),5.01±2.21 ng/ml (female), 3.77±1.41 ng/ml (male), 5.01±1.61ng/ml (female). P-value was 0.3875 (male), 0.2387 (female), 0.3028 (male), 0.169 (female) which was of no significant statistical difference .table 4.

Serum IgE:

Table 5 shows the study of IgE in the case groups and control group, the mean of serum IgE was significantly higher in the groups asthma with normal weight, asthma with overweight, asthma with metabolic syndrome and allergic rhinitis group than in control group; the mean was 215.873±138.5 Iu/ml, 261.758±144.42 Iu/ml, 207.103 ±125.515 Iu/ml, 110.626±39.353 Iu/ml for the case groups respectively and it was 82.687±34.4 Iu/ml; P-value was <0.0001 for asthma with normal weight, asthma with overweight and asthma with metabolic syndrome and it was < 0.0002 for allergic rhinitis with overweight. The mean of IgE in allergic rhinitis with normal weight group was 99.093±39.03 Iu/ml and of non

significant statistical difference than of control subjects, P-value 0.3116.

Table 6 shows the study of total serum IgE in the case and control groups according to gender distribution, mean was significantly higher in asthma with normal weight (male and female),asthma with over weight (male and female), asthma with metabolic syndrome (male and female), allergic rhinitis with normal weight (female) ,allergic rhinitis with over weight (male) groups than in control group, while it has no statistically significant difference in allergic rhinitis with normal weight male, allergic rhinitis with overweight female groups than in control group.

Body Mass Index

Table 7 shows BMI study. Mean of BMI of the case groups asthma with overweight ,asthma with metabolic syndrome and allergic rhinitis with overweight are significantly higher than of the control group; mean was 30.829± 4.041 kg/m^2 , 32.983± 4.93 kg/m^2 , 29.166± 2.804 kg/m^2 for the mentioned case group respectively and 22.091± 2.22 kg/m^2 for the control group; P-value was less than 0.0001 for all the groups. There is no significant difference between mean of the asthma with normal weight and allergic rhinitis with normal weight group, mean was 21.34± 2.54 kg/m^2 and 21.453± 2.355 kg/m^2 . P-value was 0.1015 and 0.1543 respectively.

In the study of BMI with gender distribution the subgroups of asthma with overweight, asthma with metabolic syndrome and allergic rhinitis with overweight were showing extreme significant difference than of control group and mean was 30.75± 4.464 kg/m^2 (male), 31.32± 3.773 kg/m^2 (female); 30.5± 5.592 kg/m^2 , 33.6± 4.607 kg/m^2 ; 28.41± 2.898 kg/m^2 , 29.41± 2.768 kg/m^2 to the mentioned respectively and mean of the control group was 22.03± 2.176 kg/m^2 (male) and 22.13± 2.57 kg/m^2 (female), P-value was less than 0.0001 for all groups . asthma with normal weight, allergic rhinitis with normal weight subgroups showing no significant difference and mean was 20.58± 2.476 kg/m^2 (male), 22.1± 2.405 kg/m^2 (female); 21.65± 2.309 kg/m^2 , 21.21± 2.484 kg/m^2 respectively. P-value was 0.0218, 0.9648; 0.5251, 0.2071. Table 8.

Forced Expiratory Volume at First Second (FEV_1):

In study of FEV_1 the mean of all the groups included in the study asthma with normal weight, asthma with overweight, asthma with metabolic syndrome, allergic rhinitis with normal weight and allergic rhinitis with overweight were significantly lower than that of the control group; the means were 51.48±18.406; 39.53±14.94; 45.857±18.315; 81.129±129; 73.083±10.412 for the case groups mentioned above respectively, mean of the control group was 83.333±4.861. P-value for all the groups was less than 0.0001 except for allergic rhinitis with normal weight which was 0.0310. Table 9.

Table 10 shows FEV_1 according to gender distribution : asthma with normal weight, asthma with overweight, asthma with metabolic syndrome, allergic rhinitis with normal weight and allergic rhinitis with overweight; all male and female subgroups have significant difference than that of control group except the male subgroup in allergic rhinitis with normal weight group which has no significant difference. Mean of the groups were 51.9±18.98(male), 51±18.1(female); 39.3 ±16.79, 39.6±14.22; 47.8±17.29, 45.3±18.74; 79.8±4.8, 82.54±3.41; 73.1±8.91, 73±10.98 for the case groups respectively and mean P-value for male subgroup of allergic rhinitis with normal weight group was 0.0792, for female subgroup of same group was 0.0154 and for male subgroup of allergic rhinitis with

overweight was 0.0002, the others was less than 0.0001.

Odd Ratio (Risk Factor):

Odd ratios were with significant values for HDL parameter in the three groups for both gender and total cases. Table 11.

Table (1): Distribution of study individuals by gender among the case and control groups.

Gender	Asthma			Allergic rhinitis		Control	Total
	Normal weight	Over Wight& obesity	Metabolic syndrome	Normal weight	Over weight		
Male	34	20	12	32	12	26	136(39%)
Female	36	44	44	30	36	22	212(61%)
Total	70	64	56	62	48	48	348(100%)

Table (2): Age distribution of the study individuals:

Age distribution (years)	Male	Female	Total	Percent%
16-20	22	38	60	17.24%
21-30	6	46	82	23.56%
31-40	40	60	100	28.73%
41-50	23	37	60	17.24%
51-60	15	31	46	13.21%
Total	136	212	348	100%

Table (3): Serum Leptin in case and control groups.

Variable	Asthma With Normal weigh	Asthma With Over weight	Asthma With Metabolic Syndrome	Allergic rhinitis with normal weight	Allergic R. with overweight	Control
	Total (70)	Total (64)	Total (56)	Total (62)	Total (48)	Total (48)
Mean	4.88	12.97	18.9	4.374	13.783	4.31
Median	4.8	12.95	18.9	4.7	14.5	3.8
S.D	2.61	5.095	9.271	1.626	4.929	1.576
P. V	0.1789	0.0001	0.0001	0.9360	0.0001	

Table (4): Serum Leptin in case and control group according to gender distribution:

	Asthma With Normal weigh		Asthma With Over wt.		Asthma With Metab. Synd.		Allergic rhinitis with normal Wt.		Allergic R. with over wt.		Control	
	M(34)	F(36)	M(20)	F(44)	M(12)	F(44)	M(32)	F(30)	M(12)	F(36)	M(26)	F(22)
Mean	4.75	5.01	8.93	14.76	12.53	18.35	3.77	5.01	10.56	14.85	4.18	4.34
median	4.8	4.9	6.95	13.5	13.05	22.25	4.3	5.3	10.05	16.05	3.8	3.71
S.D	3.03	2.21	3.76	4.52	4.61	9.856	1.41	1.61	5.13	4.42	1.59	1.84
P. V	0.3875	0.2387	<0.0001	<0.0001	<0.0001	<0.0001	0.3028	0.1690	<0.000	<0.0001		

Table (5): Total serum IgE in case and control groups:

Variable	Asthma With Normal weigh	Asthma With Overweight.	Asthma With Metabolic Syndrome.	Allergic Rhinitis with normal weight	Allergic Rhinitis with overweight	Control
	Total(70)	Total(64)	Total(56)	Total(62)	Total (48)	Total(48)
Mean	215.873	261.758	207.103	99.093	110.626	82.687
Median	158	187.8	152.3	99.3	110.15	77.65
S.D	138.5	144.42	125.515	39.03	39.353	34.4
P. V	<0.0001	<0.0001	<0.0001	0.3116	0.0002	

Table (6): Total serum IgE in case and control group according to gender distribution:

Variable	Asthma With Normal weigh		Asthma With Overweight		Asthma With Metabolic Syndrome		Allergic rhinitis with normal Weight		Allergic Rhinitis with overweight		Control	
	M(34)	F(36)	M(20)	F(44)	M(12)	F(44)	M(32)	F(30)	M(12)	F(36)	M(26)	F(22)
Mean	198.712	233.035	293.718	246.474	277.567	189.48	85.36	82.989	104.43	112.91	79.50	86.9
Median	122.7	171.8	320	163.6	208	149.25	102	77.55	92	113.6	77	80
S.D	158.598	114.835	146.982	142.24	136.78	117.52	36.27	36.524	35.465	40.900	37.151	31.399
P. V	0.0469	0.0127	0.0004	<0.0001	<0.0001	<0.0001	0.5540	0.0002	0.0184	0.6914		

Table (7): BMI in case and control groups:

	Asthma With Normal weight	Asthma With Overweight	Asthma With Metabolic Syndrome	Allergic rhinitis with normal Wt.	Allergic R. with overweight	Control
	Total(70)	Total(64)	Total(56)	Total(62)	Total(48)	Total(48)
Mean	21.34	30.829	232.983	21.453	29.166	22.091
Median	21.5	29	33	21	29	22.75
S.D	2.54	4.041	4.93	2.355	2.804	2.22
P. V	0.1015	<0.0001	<0.0001	0.1543	<0.0001	

Table (8): BMI in case and control group according to gender distribution:

	Asthma With Normal weigh		Asthma With Overweight		Asthma With Metabolic Syndrome		Allergic rhinitis with normal Weight		Allergic R. with overweight		Control	
	M(34)	F(36)	M(20)	F(44)	M(12)	F(44)	M(32)	F(30)	M(12)	F(36)	M(26)	F(22)
Mean	20.58	22.1	30.75	31.32	30.5	33.6	21.65	21.21	28.41	29.41	22.03	22.13
Median	18.6	23	29	31	28.25	33	22.5	20	27.5	29	23	24
S.D	2.476	2.405	4.464	3.773	5.592	4.607	2.309	2.484	2.898	2.768	2.176	2.57
P. V	0.0218	0.9648	<0.0001	<0.0001	<0.0001	<0. 0001	0.5251	0.2071	<0.0001	<0.0001		

Table (9): FEV_1 in case and control groups:

	Asthma With Normal weigh	Asthma With Overweight	Asthma With Metabolic Syndrome	Allergic rhinitis with normal weight	Allergic R. with overweight	Control
	Total (70)	Total (64)	Total (56)	Total (62)	Total (48)	Total (48)
Mean	51.48	39.53	45.857	81.129	73.083	83.333
Median	45	39.5	42	80	7.5	82
S.D	18.406	14.94	18.315	4.31	10.412	4.861
P. V	<0.0001	<0.0001	<0.0001	0.0310	<0.0001	

Table (10): Forced expiratory flow rate of first second (gender distribution):

	Asthma With Normal weigh		Asthma With Over wt.		Asthma With Metab. Synd.		Allergic rhinitis with normal Wt.		Allergic R. with over wt.		Control	
	M(34)	F(36)	M(20)	F(44)	M(12)	F(44)	M(32)	F(30)	M(12)	F(36)	M(26)	F(22)
Mean	51.9	51	39.3	39.6	47.8	45.3	79.8	82.54	73.1	73	82	84.9
Median	45	46.5	35	41	42	40	80	82	77	72.5	81	84
S.D	18.98	18.10	16.79	14.22	17.29	18.74	4.80	3.41	8.91	10.98	4.48	4.90
P. V	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0792	0.0154	0.0002	<0.0001		

Table (11): Odd ratio.

Groups		Parameters						
		Leptin (ng/ml)	Total IgE (Iu/ml)	Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	FEV1
Asthma with normal weight & asthma with over weight	M	0.106	0.3266	0.0976	0.0571	10.847	0.0571	0.5517
	F	0.0662	0.9761	0.1057	0.104	15.387	0.0792	0.2645
	T	0.0859	0.6285	0.1046	0.0835	12.770	0.0728	0.3576
Asthma with normal weight &asthma with metabolic syndrome	M	0.0858	0.0791	0.0366	0.0166	8.7966	0.0166	0.9354
	F	0.076	1.7679	0.0352	0.0594	12.9697	0.0625	0.5046
	T	0.0936	0.8014	0.0553	0.0418	10.3123	0.0492	0.594
Allergic rhinitis with normal and allergic rhinitis with over weight	M	0.0224	0.3221	0.0734	0.1529	7.314	0.335	0.6033
	F	0.0365	0.7412	0.123	0.1215	9.5606	0.2503	0.1906
	T	0.0346	0.5983	0.1037	0.1205	8.2038	0.2624	0.3032

Discussion

In this study BMI is significantly higher in asthmatic patients with obesity and overweight, asthmatic with metabolic syndrome and allergic rhinitis patients with overweight, than of control subjects. However, there was a non significant difference between men and women. In recent years, numerous prospective studies [7] have been carried out and most of prospective studies show that obesity is risk factor for the de novo diagnosis of asthma, with the risk increasing between 1.1- fold and 3-fold [7-9]. In recent cohort study including 591 adults who were monitored for 20 years found an association between asthma and obesity, but multivariate analysis revealed that asthma was a risk factor for obesity and not the other way round. [10].

Studies carried out in the pediatric population are much more heterogeneous both in terms of the strength of their results and in the direction of the asthma – obesity relationship. One study [11] of 9828 children aged between 6 and 14 years who were followed for 5 years showed that obesity increased the risk of suffering from asthma, a trend that was particularly pronounced in girls (those in the top quintile of adiposity had a 2.2-times greater risk of incident asthma in subsequent years). However, another study [12] carried out at practically the same time with the participation of 3792 children found that overweight and obesity increased the risk of bronchial asthma, more so in boys than in girls.

Leptin Role in Obesity – Asthma Relationship

The increase of asthma has paralleled the rising obesity during the past decades [13]. Obesity is characterized by the increase of leptin in the circulation. Leptin is an obesity gene product, and it can stimulate the production of pro-inflammatory mediators, such as tumor necrosis factor (TNF)-α, interleukin (IL)-6 and interferon (IFN)-γ. There is a link between leptin and asthma, especially in children. It remains unclear

however, if leptin is in the pathway of obesity- asthma relationship and if it plays a distinctive role in asthma in obese vs. non-obese subject. Since leptin is in a positive feedback loop with the pro-inflammatory cytokines such as TNF-α, there is a possibility that leptin is involved as a regulatory rather than an etiologic mechanism of asthma development. Weight loss is associated with decreased circulating leptin concentration in children. Weight control program may need to be considered in the treatment of asthma in obese children [14].

Leptin is one of the adipose-derived energy regulating hormones and an obesity gene product [15]. Circulating leptin is positively correlated with body fat percentage and body fat mass [16-18].

Figueroa – Munoz showed that asthma diagnosis and BMI were positively associated [19]. Gilliland et al. showed that the risk for new-onset asthma was higher among obese children, and found this correlation to be stronger in boys [20]. Kohrt et al.[21] studied the effects of a nine month exercise programme (walking, jogging, steps climbing) and hormonal substitutional therapy on the serum leptin level in older women. In persons who exercised, the change of body fat significantly correlated with changes in the leptin serum concentration. The effect of exercise therefore seems to be dependent on changes of the amount of body fat.

Evaluation of Total Serum IgE:

The present study showed that there is significant difference between total IgE (mean + S.D) of both gender in all asthmatic groups than mean ± S.D of the control group. For allergic rhinitis groups; the allergic rhinitis with normal weight female group showed significant difference while male group was showing no significant difference, in opposite to allergic rhinitis with overweight that male group showing significant difference and female group was showing no significant difference than that of control.

Differentiation of B cells into IgE-secreting plasma cells is a complex cascade of events in which cytokines play a crucial role [22]. Both IL-4 and IL-13 are inducing IgE synthesis whereas IFN-gamma and IL-12 are blocking IgE synthesis. IgE production by B cells not only requires the presence of IL-4 or IL-13, but also a physical interaction between T and B cells, involving a number of surface and adhesion molecules such as CD40-CD40L and CD28/CD80. production of TH-cytokines is not restricted to T cells as basophils and mast cells can produce them indicating that these cells may be of importance in the synthesis of IgE [23].

Population studies have shown an association between prevalence of asthma or bronchial hyperrespinsiveness and total serum IgE levels [24,25], independent of specific reactivity to common allergens or symptoms of allergy [26].

The mean serum IgE levels in asthmatic patients as this study indicated was lower than that reported by Chowdary et al. [27] which is 700IU/ml and Ghin et al [28] which is 676.08 IU/ml. Al-Amri et al. reported a geometric mean of serum IgE of 468 IU/ml for Omani asthmatic patients [29]. Other studies reported lower wide range of serum mean IgE level in asthmatic patients from 190 IU/ml to 394.9 IU/ml [30,31,32]. The variety in mean serum IgE levels between the above reported studies may be influenced by allergen exposure magnitude in different geographical areas.

Conclusion

Leptin was significantly higher in patients with asthma and allergic rhinitis as compared to healthy non allergic individuals and it was influenced by BMI and presence of metabolic syndrome in allergic patients.

BMI influence FEV 1 in both asthmatic and allergic rhinitis patients.

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