

Study on serum Leptin level of children with Asthma

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Abstract: Based on epidemiological studies, incidence of asthma and obesity is rising in parallel and the obesity is associated with severe asthma and its poor medical treatment response. The changes in immune system function by means of some mediators like Leptin is effective in coincidence asthma and obesity. The aim of this study was evaluation of Leptin levels in children with asthma and its relation with treatment and the affected children's Body mass index (BMI). In a cross sectional descriptive analytic study in pediatric disease department of Tabriz university of medical sciences, we evaluated the serum level of Leptin in children with asthma. The Leptin level in patients with asthma was 29.60 ± 29.25 and in control group was 6.34 ± 6.52 respectively which was significantly higher in the case group ($P < 0.001$). Serum level of Leptin in patients with periodic asthma was 9.26 ± 10.90 and in patients with persistent asthma was 36.74 ± 30.38 that Serum level of Leptin was significantly higher in patients with persistent asthma than periodic asthma ($P < 0.001$) and also Serum level of Leptin in patients with severe persistent asthma was 46.97 ± 33.88 that significantly higher ($P < 0.001$). Mean of serum level of Leptin in patient's with good response to treatment was 9.26 ± 10.90 , in patient's with moderate response to treatment was 22.74 ± 21.12 and in patient's with poor response to treatment 40.01 ± 29.25 that significantly higher in patient's poor response to treatment ($P = 0.004$). In patients with asthma, a significant positive linear correlation was found between Serum level of Leptin with age, height, weight, weight Percentile-for-age and BMI. In patients of control group, a significant positive linear correlation was found between Serum level of Leptin with weight, Weight Percentile-for-age, BMI, BMI Percentile-for-age and BMI z-score-for-age.

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Keywords: Asthma, Leptin; Body mass index (BMI); Response to Treatment

1. Introduction

Based on epidemiological studies, incidence of asthma and obesity is rising in parallel (Ford, 2005) and the obesity is associated with severe asthma and its poor medical treatment response (Taylor, 2008).

The cause of coincidence of asthma with obesity is not defined exactly but the possible mechanisms included; life style with low mobility, nutritional factors, hormonal factors, systemic inflammation and reduced respiratory capacity due to obesity, insulin resistance, and Gastroesophageal reflux. The changes in immune system function by means of some mediators like Leptin is effective in coincidence asthma and obesity (Jartti, 2009).

Leptin is made by the adipose tissue cells and their serum level is associated with BMI and the thickness of skin folds especially in women. Leptin affects on production of different neuropathies by means of hypothalamus axis and this also affects energy production and consumption and neuroendocrine function, in the other hand Leptin is a modulator of the immune system and is a proinflammatory state in the body.

Leptin causes to increase in production of TNF- α and IL-6 by adipose tissue cells and amplifies the T –

Helper cells and has a role in asthma pathogenesis by this mechanism.

The association of Leptin and asthma have been evaluated in several studies, in a cross sectional study by Asood and colleague, it was found that the increased Leptin levels are associated with an increased incidence of asthma in women (Sood, 2006).

Camargo and colleague have shown that there is higher risk for asthma in 4 upcoming years in women who gain weight after the age of 18 (Castro-Rodríguez, 2007) and there is no significant relation between asthma incidence and the used calorie and physical activity (Camargo, 1999).

Rodríguez and colleagues stated that overweight and obesity increase the risk of asthma in females from 6 to 11 years old up to 7 times (Castro-Rodríguez, 2001).

Mai and colleagues stated that the level of Leptin in overweight children with asthma is two times more than children with asthma with normal weight (Mai, 2004).

Culer and colleagues investigated the role of Leptin in childhood asthma, and stated that a Leptin level in children with asthma is high and there is not

a relationship between serum Leptin and obesity in these children (Guler, 2004).

With regard to the fact that asthma and its recurrent attacks has a psychological and economic burden on the family and the serum levels of Leptin plays a role in childhood asthma and its response to medical treatment and the serum levels of Leptin is not measured in children with asthma yet, we designed a study to evaluate the Leptin levels of children with asthma and its relation with treatment and the affected children's BMI.

2. Material and Methods

In a cross sectional descriptive analytic study in pediatric disease department of Tabriz university of medical sciences, we evaluated the serum level of Leptin in children with asthma.

With simple sampling method, we studied all the children with asthma referring to pulmonology clinic of Tabriz children's hospital or Tabriz Azadi clinic after achieving the inclusion and exclusion criterias.

The inclusion criterias include:

- 1-Age below 12 yrs
- 2-At least 1 year from the time of diagnosis
- 3- No other underlying disease
- 4- Lack of acute infection within past 2 weeks
- 6 - Having a high BMI more than 5 percentiles of age and gender.
- 7 - Not receiving other drugs (except anti asthma drugs) in the last 6 months

Children with above criteria were enrolled to the study with informed consent

We enrolled 50 children to the study with asthma after achieving inclusion and exclusion criterias as the case group and a group of 50 healthy children who were selected by age and Sex matched without acute and chronic inflammatory diseases or infections that had no drug using history as control group. Accurate measurements of weight and height are done by Seca stadiometer.

After an overnight fasting (at least 8 hours), venous blood samples obtained from patients with Low-speed centrifugation serum was isolated in the laboratory and was freezes at -70 degrees Celsius in Eppendorf vials .Measurement of Serum Leptin was done with ELISA method using LDN Leptin ELISA Kits.

The number of asthma attacks and asthma severity was determined based on GINA 2008 protocol.

NCHS standard curves were used for converting height and weight to standard Deviation Score (SDS). The BMI percentile in the case and control group was also defined with regard to the age and sex BMI percentiles.

Statistical analysis:

All data were analyzed using descriptive and deductive statistics methods by SPSS Ver. 15. The relation between qualitative data was evaluated using Chi-square test. And the relation between quality and quantity data were evaluated using T-test, ANOVA tests and the relation between the variables were evaluated using Pearson and Spearman correlation coefficient. $P < 0.05$ was considered meaningful.

Table 1. Demographics parameter of patients between two groups

	Group			
	Case		Control	
	Male	Female	Male	Female
Age	31	19	31	19
Height	66.70 ± 33.05	65.44 ± 33.26	0.850	
Height Percentile-for-age	112.74 ± 18.23	112.09 ± 18.60	0.860	
Height z-score-for-age	56.29 ± 31.89	56.74 ± 32.51	0.944	
Weight	0.27 ± 1.15	0.26 ± 1.24	0.985	
Weight Percentile-for-age	26.05 ± 12.16	25.43 ± 11.26	0.791	
Weight z-score-for-age	79.75 ± 23.79	79.15 ± 24.39	0.904	
BMI	1.57 ± 1.61	1.59 ± 1.79	0.942	
BMI Percentile-for-age	19.54 ± 4.39	19.45 ± 4.33	0.917	
BMI z-score-for-age	80.50 ± 24.79	80.88 ± 25.84	0.940	
	1.89 ± 1.87	1.96 ± 2.05	0.855	

Table 2. Evaluation of age, height, weight and BMI based on response to treatment in patients with asthma

	Response to treatment			P
	Good	Moderate	Poor	
Age	65.38 ± 32.49	86.14 ± 41.32	62.73 ± 30.78	0.241
Height	111.00 ± 16.30	119.07 ± 21.11	112.02 ± 18.64	0.613
Height Percentile-for-age	53.45 ± 25.36	42.16 ± 36.05	60.81 ± 33.32	0.361
Height z-score-for-age	0.14 ± 0.83	-0.32 ± 1.32	0.46 ± 1.21	0.246
Weight	21.92 ± 10.16	33.79 ± 18.84	26.04 ± 10.56	0.114
Weight Percentile-for-age	64.79 ± 25.21	66.34 ± 32.36	88.26 ± 17.52	0.004
Weight z-score-for-age	0.67 ± 1.24	1.08 ± 1.94	2.03 ± 1.55	0.033
BMI	17.14 ± 3.89	21.79 ± 6.01	20.05 ± 3.85	0.044
BMI Percentile-for-age	61.20 ± 25.08	88.03 ± 17.93	87.11 ± 22.05	0.003
BMI z-score-for-age	0.68 ± 1.52	2.14 ± 1.55	2.36 ± 1.89	0.022

Table 3. Birth weight, Mother age at labor and Onset of asthma BMI based on response to treatment in patients with asthma

	Response to treatment			P
	Good	Moderate	Poor	
Birth weight	3.12 ± 0.49	3.07 ± 0.33	3.24 ± 0.43	0.510
Mother age at labor	27.23 ± 5.07	23.29 ± 4.35	24.30 ± 4.70	0.122
Onset of asthma	45.43 ± 18.20	45.86 ± 35.44	38.33 ± 30.85	0.687

3. Results

We studied the serum levels of Leptin in 50 Asthmatic patients with 50 healthy patients as control group. The two groups were matched for age, gender, weight and height. The demographic findings of both groups are shown in the table 1. Thirty one of patients in each group were male and 19 of them were female ($P=1$).

Mean age of patient's with asthma was 66.70 ± 33.05 month and in control group was 65.44 ± 33.26 month ($P=0.850$).

The Leptin level in patients with asthma was 29.60 ± 29.25 and in control group was 6.34 ± 6.52

respectively which was significantly higher in the case group ($P < 0.001$) (Figure 1).

The family history of asthma was positive in 58% and 2% of asthmatic and non asthmatic patients, respectively that positive family history of asthma was significantly more in case group ($P < 0.001$).

Evaluations of studied parameter based on response to treatment in patients with asthma were shown in tables 2 and 3.

Serum Leptin level of patients with asthma based on multi drug usage were shown in table 4. The demographic findings of both groups based on patient's gender are shown in the table 5.

Thirteen of asthmatic patients had periodic asthma and 37 of them had persistent asthma that of 37 patients with persistent asthma, 2 patients had mild persistent asthma, 13 patients had moderate asthma and 22 patients had severe persistent asthma. Serum level of Leptin based on asthma type was shown in figure 2 and serum level of Leptin in patients with periodic asthma was 9.26 ± 10.90 and in patients with persistent asthma was 36.74 ± 30.38 that Serum level of Leptin was significantly higher in patients with persistent asthma than periodic asthma ($P < 0.001$) and also Serum level of Leptin in patients with severe persistent asthma was 46.97 ± 33.88 that significantly higher ($P < 0.001$).

In patients with asthma, a significant positive linear correlation was found between Serum level of Leptin with age ($P = 0.025$ and $R = 0.317$), height ($P = 0.006$ and $R = 0.380$), weight ($P = 0.003$ and $R = 0.4127$), Weight Percentile-for-age ($P = 0.007$ and $R = 0.393$) and BMI ($P = 0.033$ and $R = 0.302$).

In patient's of control group, a significant positive linear correlation was found between Serum level of Leptin with weight ($P = 0.015$ and $R = 0.344$), Weight Percentile-for-age ($P = 0.017$ and $R = 0.350$), BMI ($P = 0.004$ and $R = 0.398$), BMI Percentile-for-age ($P = 0.016$ and $R = 0.338$) and BMI z-score-for-age ($P = 0.005$ and $R = 0.391$).

Mean of serum level of Leptin in patient's with good response to treatment was 9.26 ± 10.90 , in patient's with moderate response to treatment was 22.74 ± 21.12 and in patient's with poor response to treatment 40.01 ± 29.25 that significantly higher in patient's poor response to treatment ($P = 0.004$) (Figure 2).

4. Discussions

Obesity leads to more severe asthma symptoms in children (Yuksel, 2012). Asthma is linked with obesity in adults, but our results do not support a significant role for Leptin, adiponectin or any other obesity-related biomarker studied in this association (Jartti, 2009). The prevalence of asthma and obesity is increasing concomitantly (Jartti, 2009). The

prevalence of asthma and obesity is increasing concomitantly, but many aspects of this link are unclear (Jartti, 2009).

Obesity is suggested as a risk factor for asthma, but the mechanisms are unclear (Mai, 2004). Obesity is not a factor in the ability to control asthma (Kwong, 2006). Adiposity is associated with poorer asthma control in female subjects. Adiponectin is associated with improved asthma control in male subjects (Kattan, 2010).

Table 4. Serum Leptin level of patients with asthma based on multi drug usage

		Leptin level	P
Ketotifen	Yes	116.40	0.002
	No	27.83 ± 26.71	
Theophylline	Yes	116.40	0.002
	No	27.83 ± 26.71	
cromolyn sodium Spray	Yes	89.80 ± 37.62	0.002
	No	27.10 ± 26.48	
Salbutamol Spray	Yes	27.63 ± 26.95	0.018
	No	76.95 ± 55.79	
Flixotide Spray	Yes	24.55 ± 20.55	0.202
	No	36.04 ± 37.09	
Serevent Spray	Yes	32.28 ± 33.69	0.781
	No	29.10 ± 28.76	
Hydrocortisone	Yes	39.10	0.747
	No	29.41 ± 29.52	
Atrovent Spray	Yes	28.64 ± 32.59	0.882
	No	29.94 ± 28.46	
Montelukaste	Yes	0.30	0.317
	No	30.20 ± 29.24	
Ventolin	Yes	32.30	0.927
	No	29.55 ± 29.55	

Obesity leads to more severe asthma symptoms in children. Moreover, Leptin, adiponectin, and ghrelin may play important roles in the inflammatory pathogenesis of asthma and obesity co-morbidity (Jartti, 2009). Moreover, Leptin, adiponectin, and ghrelin may play important roles in the inflammatory pathogenesis of asthma and obesity co-morbidity (Yuksel, 2012).

Leptin is an obesity gene product secreted by white adipose tissue; elevated serum levels are found in obese adults and children. Recently, Leptin has also been found to be associated with allergic rhinitis (AR) (Quek, 2010). Leptin might be involved in the pathogenesis of asthma in the overweight children, and IFN-gamma might be a pathway in the process of leptin-induced inflammation (Mai, 2004).

Leptin could aggravate airway inflammation featured by infiltration of neutrophils and enhancement of Th1 type inflammation (Cao, 2009). Leptin, via proliferation and activation of Th2 cells, may induce inflammation in asthma. It has also been demonstrated that Leptin mRNA expression and protein levels increase in response to inflammatory stimuli (Szczepankiewicz, 2009).

Table 5. Evaluation of parameter based patient's gender in each group

	Group					
	Case			Control		
	Male	Female	P	Male	Female	P
Leptin	30.16 ± 25.33	28.69 ± 35.48	0.865	6.47 ± 6.42	6.13 ± 6.87	0.882
Age(month)	70.45 ± 35.34	60.58 ± 28.78	0.310	67.68 ± 35.99	61.79 ± 28.81	0.549
Height	114.32 ± 17.72	110.16 ± 19.22	0.439	113.06 ± 19.09	110.50 ± 18.17	0.641
Height Percentile-for-age	55.79 ± 30.95	57.09 ± 34.21	0.891	55.65 ± 31.99	58.52 ± 34.14	0.765
Height z-score-for-age	0.18 ± 1.07	0.41 ± 1.28	0.501	0.20 ± 1.26	0.36 ± 1.24	0.667
weight	27.78 ± 12.18	23.24 ± 11.90	0.203	27.61 ± 12.20	21.88 ± 8.68	0.080
Weight Percentile-for-age	84.07 ± 21.82	73.63 ± 25.67	0.145	82.20 ± 24.76	74.81 ± 23.84	0.317
Weight z-score-for-age	1.92 ± 1.72	1.06 ± 1.32	0.073	2.10 ± 2.07	0.87 ± 0.93	0.009
BMI	20.45 ± 4.51	18.06 ± 3.87	0.061	20.75 ± 4.59	17.33 ± 2.90	0.002
BMI Percentile-for-age	85.37 ± 23.21	72.55 ± 25.85	0.076	85.19 ± 24.98	73.86 ± 26.35	0.134
BMI z-score-for-age	2.38 ± 1.99	1.10 ± 1.35	0.017	2.61 ± 2.25	0.91 ± 1.07	0.001
Birth weight	3.24 ± 0.44	3.10 ± 0.41	0.260	3.21 ± 0.44	3.07 ± 0.52	0.355

Levels of the adipocyte-derived hormones Leptin and adiponectin are significantly correlated with bronchial hyperresponsiveness (BHR) induced by exercise challenge in children with asthma (Baek, 2011). Szczepankiewicz and colleague demonstrate that increased serum Leptin levels have been observed in asthmatic patients (Szczepankiewicz, 2009). Guler and colleague demonstrate that A significant difference was observed in serum Leptin levels between asthmatic and healthy children (Guler, 2004).

In our study, serum Leptin level in patients with asthma was 29.60 ± 29.25 and in control group was 6.34 ± 6.52 and serum Leptin level in patients with asthma was significantly higher than healthy patients.

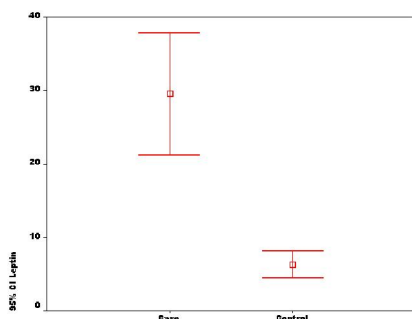


Figure 1. Distribution of serum Leptin level in both groups

Tanju and colleague show that Leptin levels correlated with the clinical severity of asthma and this was suggested to be associated with the severity of inflammation in asthma (Tanju, 2011). Data of Erel and colleague study demonstrate that the serum levels of Leptin and lipid profiles on allergic rhinitis and mild asthma were not different than those in controls (Erel, 2007).

In our study, Serum level of Leptin was significantly higher in patients with persistent asthma than periodic asthma ($P < 0.001$) and also Serum level of Leptin in patients with severd persistent asthma was 46.97 ± 33.88 that significantly higher ($P < 0.001$).

Szczepankiewicz show that polymorphisms of the Leptin gene may be associated with asthma and higher BMI in asthmatic patients (Szczepankiewicz, 2009).

In our study and in patients with asthma, a significant positive liner correlation was found between Serum level of Leptin with weight ($P = 0.003$ and $R = 0.4127$), Weight Percentile-for-age ($P = 0.007$ and $R = 0.393$) and BMI ($P = 0.033$ and $R = 0.302$).

Guler and et al show that there was no significant sex difference in serum Leptin levels among asthmatic children, whereas healthy boys had significantly lower Leptin levels than healthy girls ($P = .019$) (Guler, 2004).

In my study significant difference was not found in Serum level of Leptin by patient gender in patients with and without asthma.

The results of Quek and colleague study indicate that a higher serum Leptin level has stronger association with mild-to-moderate persistent asthma compared with allergic rhinitis. Hence, serum Leptin may be a stronger predictor for childhood asthma compared with allergic rhinitis. Among the asthmatic children, higher serum Leptin levels also showed stronger associations with female gender and being overweight (Quek, 2010).

In our study, Serum level of Leptin significantly higher in patient's poor response to treatment and severd persistent asthma.

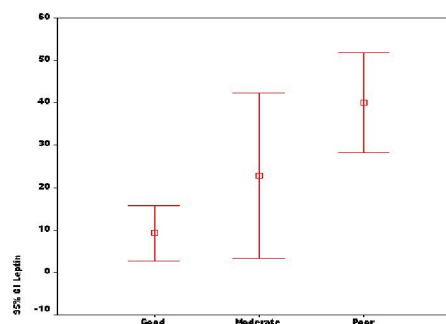


Figure 2. Distribution of serum Leptin level based on response to treatment in patient's with asthma

Conclusion

The Leptin level in patients with asthma was 29.60 ± 29.25 and in control group was 6.34 ± 6.52 and significantly higher in patients with asthma. Serum level of Leptin in patients with periodic asthma was 9.26 ± 10.90 and in patients with persistent asthma was 36.74 ± 30.38 that Serum level of Leptin was significantly higher in patients with persistent asthma and also significantly higher in patients with severe persistent asthma. Serum level of Leptin was significantly higher in patients with poor response to treatment.

In patients with asthma, a significant positive linear correlation was found between Serum level of Leptin with age, height, weight, weight Percentile-for-age and BMI.

In patients of control group, a significant positive linear correlation was found between Serum level of Leptin with weight, Weight Percentile-for-age, BMI, BMI Percentile-for-age and BMI z-score-for-age.

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