

Effect of alpha-1 antitrypsin, adiponectin, leptin in obesity

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PhD

Summary:

Background:- Obesity is associated to significant disturbances in endocrine function. Hyper insulinemia and insulin resistance are the best known changes in obesity, but their mechanisms and clinical significance are not clearly established.

Objectives:- to investigate the relationship between alpha-1 antitrypsin, leptin, adiponectin in serum of an obese population to find new markers for treating obesity and related disease.

Patients and methods:- This study had included thirty patients with obese (12 male and 18 female) with age ranged between 30-45 years and thirty apparently subjects matched for age and weight have been studied, attending the out patients consultation clinic of Baghdad teaching hospital in medical city. The levels of A1AT, adiponectin, leptin, within the centrifuged samples were tested using the ELISA kits purchased from the Millipore Corporation.

Results:- Result obtained in the present study showed that serum levels of alpha-1 antitrypsin and adiponectin were significantly lower in obese patients than in healthy control. while the serum level of leptin was significantly higher in obese patients than in healthy control.

Conclusion:- levels of alpha-1 antitrypsin in human serum correlate strongly with BMI and also with serum levels of adiponectin, and leptin. These results suggest that alpha-1 antitrypsin might be useful as a biomarker and be a potential target for treating obesity.

Key words:- alpha-1 antitrypsin, adiponectin, leptin, obesity.

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Introduction:-

Obesity is associated to significant disturbances in endocrine function. Hyper insulinemia and insulin resistance are the best known changes in obesity, but their mechanisms and clinical significance are not clearly established. Adipose tissue is considered to be a hormone-secreting endocrine organ; and increased leptin secretion from the adipocyte, a satiety signal, is a well-established endocrine change in obesity. body weight increases (1,2). Adiponectin is specifically expressed in human adipocytes. Plasma adiponectin concentration is decreased in individuals with obesity, and body-weight reduction increases. Several studies have suggested that adiponectin may have a role of glucose metabolism and insulin sensitivity. (3,4). The mechanism is adiponectin can ameliorate insulin sensitivity (4). The mechanisms include the increased peripheral glucose uptake, muscle oxidation via the activation of AMP-activated protein kinase, and the suppressed hepatic glucose production, in addition to enhancing insulin-induced tyrosine phosphorylation of the insulin receptor (IR). Leptin plays an important role in the control of food intake, energy expenditure, metabolism, and body weight. (5). This leptin resistance may be food intake and body weight, obesity is characterized by high plasma leptin levels. This leptin resistance may be the reason for high leptin levels that cannot induce the presumed reducing effects on feeding and body weight, which may relieve obesity. (5).

Some study has shown that the major function of alpha 1-antitrypsin (A1AT) is to inhibit the

excessive neutrophil elastase and other serine proteinases to maintain the physiological proteinase antiproteinase balance.

(6). Alph

has a strong vascular transparency, a higher concentration in the lung tissue when compared with the concentration of other serine protease inhibitors such as-macroglobulin. Moreover, it has a high affinity for elastase, suggesting that its primary physiological function is to inhibit elastase activity and protect the lungs from damage by elastase. A1AT is found to have many new inhibitory and non-inhibitory features involved in anti-inflammatory, immunomodulatory, and antimicrobial functions, and A1AT activity is extensive to most body tissues in addition to lungs. Recent studies have found that the expression of some proteases (such as Cathepsin K) (7,8). gradually increases with fat cell differentiation and maturation, and that inhibitors of these enzymes may affect adipocyte differentiation. The aim of the study to investigate the relationship between alpha-1 antitrypsin, leptin, adiponectin in the serum of an obese population to find new biomarkers for treating obesity and related disease.

Patients and Methods:-

This study had included thirty patients with obesity (12 male and 18 female) with age ranged between 30-45 year and thirty healthy subjects m have been studied, attending the out patients consultation clinic of Baghdad teaching hospital in medical city, in the a period from December 2012– march 2013.

The levels of A1AT, adiponectin, leptin, were tested using the ELISA kits purchased from the Millipore Corporation.

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performed the ELISA according to the protocol provided by the manufacturer, using the Health HDM_9602G ELISA analyzer (Beijing Plantier Technology Co., Ltd).

Statistical analyses:-

Descriptive statistics for all data of each set were expressed as mean ± SD and the percent of abnormal value in any test was calculated as above or below the mean ± SD of the normal value for the matched control group, were compared using independent sample (t)test p<0.05 were considered statistically significant.

The overall predictive values for the results in the studied groups were performed according to program of office xp.

Results:-

The characteristics of the study population and the obesity factors were shown in Tables 1.

Table 1 - Characteristics of the study population.

Characteristics	CONTROL (n=30) Mean ±SD	PATIENTS (n=30) Mean ±SD
Age(years)	27± 2.50	28.5±1.5
BMI(Kg/m ²)	25±5	32.5±2.5*

*p<0.05 compared to normal control.

Body mass index of patients group was significantly higher than normal control.

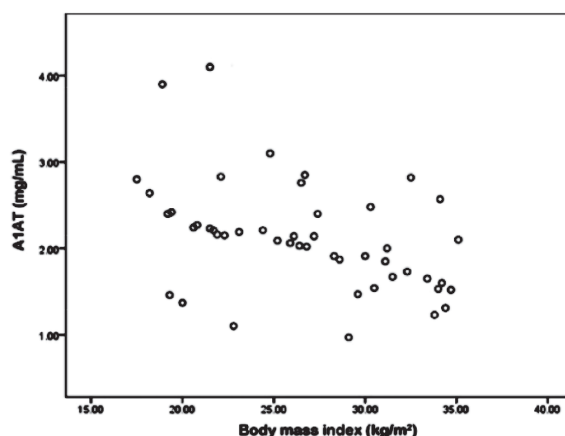
Result obtained in the present study showed that serum levels of alpha-1antitrypsin and adiponectin were significantly lower in obese patients than in healthy control(p<0.05and p<0.01) respectively .while the serum level of leptin was significantly higher in obese patients than in healthy control(p<0.05).are shown in table 2.

Table 2:- mean±SD of serum alpha-1 antitrypsin ,leptin, adiponectin in patients and healthy control.

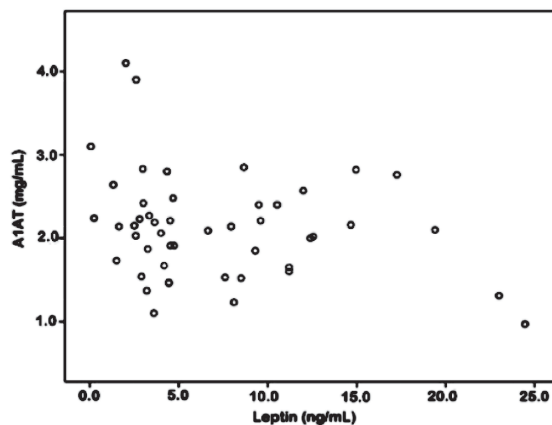
Type	control(n=30) Mean ±SD	patients(n=30) Mean±SD
Alpha-1antitrypsin (mg/ml)	2.75± 0.25	1.31±0.06**
Adiponectin(ng/ml)	8.75 ±0.75	5.25 ±0.25*
leptin(ng/ml)	4 ±0.5	9.3 ±0.3*

*p<0.05, aSignificantly diffent from control group, ***(p<0.01), Significantly diffent from control group (p<0.05).

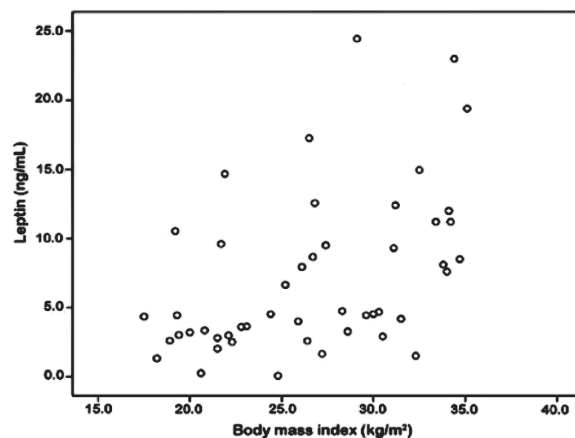
A1AT levels correlated negatively with BMI (Figure 1. r = -0.433, p=0.02). There was a negative correlation between the levels of A1AT and leptin, but this was not significant, as shown in Figure 2 (r = - 0.248, p=0.09) Leptin levels correlated positively with BMI (Figure 3(r=0.47, p=0.01).



Fig(1):- Correlation of serum alpha 1-antitrypsin (A1AT) and body and body mass index.



Fig(2):- Correlation of serum alpha 1-antitrypsin (A1AT)and leptin



Fig(3):- Correlation of serum leptin and body mass index.

Discussion:-

Obesity is associated to significant disturbances in endocrine function. Hyper insulinemia and insulin resistance are the best known changes in obesity. Previous studies have examined the relationship between obesity and serum levels of leptin, adiponectin and insulin(9). but there have been no studies on the relationship between A1AT levels and obesity. In the present study, the analyzed the correlation between serum A1AT levels and BMI as well as other factors such as serum leptin, insulin and adiponectin levels in a group population. Results obtained in the present study agree with others , like Hillon P, Guiu B,et al who found that the level of leptin was higher in patients with obese than in healthy control(10). There was a significant positive correlation between BMI and serum levels of leptin. As the product of the obese gene, leptin plays an important role in the self-stabilizing regulatory mechanism that maintains the level of body fat. Studies have shown that serum leptin levels increase with the body fat level. (11) However, leptin resistance prevents these enhanced serum leptin levels from effectively controlling the individual's weight. Therefore, measured leptin levels are important in characterizing the degree nature of an individual's and obesity (12). The present study also found that serum adiponectin levels were significantly lower in patients with obese than in healthy control Which agree with that of Rahman et al2009 who stated that serum adiponectin was significantly lower in obese patients than in healthy control . and that there was a significant negative correlation between BMI and serum adiponectin levels. Adiponectin is a plasma protein that is secreted by the adipose tissue and is closely associated with obesity, insulin resistance, type II diabetes mellitus and atherosclerosis. (13). The normal physiological levels, adiponectin promotes fatty acid oxidation and energy consumption in the liver and muscle tissues; thereby reducing intracellular triglyceride (TG) levels, and alleviating hyperlipidemia, insulin resistance, and type II diabetes in obese rats. Mallamuei et al have shown that intravenous injection of adiponectin reduces the hepatic levels of mRNAs encoding 2 glycogen forming enzymes (phosphoenolpyruvate carboxylase and glucose-6-phosphatase) that reduces endogenous glucose production. Adiponectin therefore plays an important role in regulating body weight(14). It was found that serum A1AT levels were significantly lower in the obese patients than in the healthy control and correlated negatively with BMI and leptin levels. Alpha 1-antitrypsin plays an important role in the pathogenesis of many inflammatory lung diseases the pathogenesis of many inflammatory lung diseases, such as emphysema, cystic fibrosis, acute respiratory distress syndrome, and acute/ chronic bronchitis(15,16). However, it has not previously been linked to obesity. Alpha 1-antitrypsin is a serine proteinase inhibitor that is primarily synthesized by hepatocytes and inhibits the activity of various serine endoproteinases, such as elastase, trypsin, plasmin, and thrombin. It is 40% homologous to Vaspin, another serine protease inhibitor belonging to the

serpin family(17). In conclusion, levels of alpha-1antitrypsin in human serum correlate strongly with BMI and also with serum levels of adiponectin, and leptin. These results suggest that alpha-1antitrypsin might be useful as a novel biomarker and be a potential target for treating obesity.

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