Estimation the correlation between IL-6, TGF- β1 with increase Body mass index in adults in Babil province Iraq

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Abstract

This article aims to determine the association between IL-6, TGF- β1 with increase adipose tissue represented the increase of the waist circumference and body max index in adults in both groups and sex. This case-control analysis is performed on 89 (100%) were patients with obesity 52 (58.43 %) and 37(41.57%) were control for age range from (19-40) years. The results showed that there are significant differences (P≤ 0.05) in mean of ages, which reached 29.71± 0.92 year in obese groups, while it was 23.54± 0.81 year in control groups. The results indicated that there are significant differences (P≤ 0.05) of BMI was 35.86± 0.59 Kg/M2 in obese groups and reached 22.68± 0.29 Kg/M2 in control groups, as well as, the waist circumference was higher (P≤ 0.05) in obese groups which reached 108.35± 1.91 cm, whereas it was 80.11± 1.23 cm in control groups.

There were no significant differences in these parameters among both sex of two groups. The data demonstrated that the obese groups, were no significant differences of IL-6, TGF- β1 in both sex of study groups and among three classes of obese groups. Correlation analysis showed that was no significant correlation between BMI with the levels of IL-6, TGF- β1 in obese as well as in sex" of the obese groups.

Keywords: *Body mass index, IL-6, TGF- β1, obesity.*

تقدير العلاقة بين بين مستويات انترلوكين -6 ، عامل النمو المحول بيتا واحد مع زيادة كتلة الجسم لدى البالغين في محافظة بابل

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الخلاصة

تهدف هذه المقالة إلى تحديد العلاقة بين انترلوكين IL-6، عامل النمو المحول بيتا واحد مع زيادة الأنسجة الدهنية لدى الاشخاص البدناء والمحدد من خلال قياس زيادة محيط الخصر ومؤشر كتلة الجسم لدى البالغين في كلتا مجموعتي السيطرة والمرضى ولدى مختلف الجنسين. تم إجراء تحليل الحالات والشواهد على 89 (100٪) حيث ان 52 (58.43٪) منهم كانوا مجموعه مرضى بالسمنة و 37 (41.57٪) كانوا من مجموعه الاصحاء وضمن الفئة العمرية من (19-40) سنة. أظهرت

النتائج وجود فروق ذات دلالة إحصائية ($P \leq 0.05$) في متوسط الأعمار ، والتي وصلت إلى 29.71 ± 0.92 عامًا في مجموعات السمنة ، بينما كانت 23.54 ± 0.81 عامًا في مجموعات السيطرة. كذلك وجود فروق ذات دلالة إحصائية ($P \leq 0.05$) في مؤشر كتلة الجسم 35.86 ± 0.59 كجم / م^2 لدى مجموعه المرضى بالسمنة المفرطة ووصل إلى 22.68 ± 0.29 كجم / م2 في مجموعات السيطرة ، وكذلك عند محيط الخصر التي وصلت إلى 108.35 ± 1.91 سم ، في حين كان 80.11 ± 1.23 سم في مجموعات السيطرة.

كما اوضحت النتائج بعدم وجود فروق ذات دلالة إحصائية في هذه المعايير بين كلا الجنسين من مجموعتين و لم تكن هناك فروق ذات دلالة إحصائية في انترلوكين IL-6 و عامل النمو المحول بيتا واحد في كل من جنس مجموعات الدراسة وبين الثلاث فئات من مجموعات السمنة. أظهر تحليل الارتباط بعدم وجود ارتباط كبير بين مؤشر كتلة الجسم مع مستويات انترلوكين IL-6 و عامل النمو المحول بيتا واحد لدى الاشخاص البدناء ولكلا الجنسين.

الكلمات المفتاحية: *مؤشر كتلة الجسم ، انترلوكين 6، عامل النمو المحول بيتا واحد TGF- β1 ، السمنة.*

Introduction

The free IL-6 is a single polypeptide chain composed of 185 amino acids that forms a bundle of four a-helices [1]. It is regarded as the major pro-inflammatory cytokine ,that induce liver to secret acute phase proteins [2], this proteins regulates metabolic and immunologic responses through its impact on liver, adipose tissue, adrenal-pituitary-hypothalamus axis, and leukocytes [3]. Thus IL-6 considered is a true endocrine cytokine, because that most cellular targets are distant from the site of release and the effects of IL-6 are correlated with the serum concentration [4]. The IL-6 secretion by adipose tissue contributes to energy homeostasis through an endocrine act on the CNS, then one could invoke a state of obesity-induced IL-6 resistance, such as described for the effects of obesity on leptin and insulin signaling, in addition, the possibility that increased adipose-tissue IL-6 secretion associated with obesity may be a regulatory mechanism attempting to correct excess body weight and achieve negative energy balance, as hypothesized for obesity-related increases in leptin [5] The anti-inflammatory cytokine TGF-β1 is a polypeptide member of the growth-factor superfamily of cytokines and includes at least 30 members in mammals, and all cells in rodents and humans can produce and respond to TGF-β1, also, members of the TGF superfamily control fundamental processes, such as proliferation, cell development, differentiation, motility, further cellular matrix production, death, cytoskeletal organization, cell adhesion, and migration [6].

The TGF-β1 was first discovered as a critical factor for the growth of non-immune cells, but has slowly been documented as a critical cytokine in the regulation of immune responses, which regulates immune cells that are involved in both innate and adaptive immune response, exerting its immune-suppressive effects through preventing the function of inflammatory cells and promoting the function of regulatory T cells [7].

The ranks of TGF-β1 correlate with mass of body fat. in humans [8], where TGF-β1and BMI are closely associated in human adipose tissue during morbid obesity and its elevated levels in humans correlate positively with increased adiposity and poor metabolic shape and contrariwise correlate with fitness, as evidenced by reduced oxygen consumption during greatest exercise trying, furthermore, the presence of TGF-β1 polymorphisms is correlated with predisposition to various forms of cancer, atherosclerosis, myocardial infarction, hypertension, and stroke, where TGF-β1 level on adipose tissue is strongly associated with class III obesity[9].

Materials and method

This study was conducted in department of nutrition at the Murjan teaching hospital / in Babylon province/Iraq for the period in January 2016-septemper 2018 for aged range from (19-40) years. Data were collected through exploration of questionnaires for study participation included: diagnosed as having obesity through defined of WHO for obesity and BMI in all of the obese group was above 30 kg/m2; whereas it was less than 25 kg/m2 in the control group. Excepted were patients who suffer from any chronic diseases or difference in sex hormones and thyroid, kidney disease, liver, smoking and alcohol intake.

The waist circumference was measured while the subject standing up, at the narrowest point of the torso width-wise, usually just above the belly button, which is ≤ 102 cm in male and≤88 cm in female. Three milliliters of venous blood were collected from each subject in the study. The Peptide IL-6 and TGF- β1 was measured by using specific kit (ELISA) supplied by Elascience - China company. The statistical analysis of this study was made by using SPSS program (Version 15.0) and the data are expressed as the Means, Standard Error, One –sample T Test, Correlation coefficient was performed with the BMI, the IL-6, TGF- β1. Values were considered statistically significant if the associated P values were lower than 0.05.

Results

As illustrated in Table (1), the results showed there was significant differences (P≤ 0.05) in mean of ages, which reached 29.71± 0.92 year in obese groups, while it was 23.54± 0.81 year in control groups. The BMI was 35.86± 0.59 Kg/M2 in obese groups and reached 22.68± 0.29 Kg/M2 in control groups, as well as, the waist circumference was higher ((P≤ 0.05) in obese groups which reached 108.35± 1.91 cm, whereas it was 80.11± 1.23 cm in control groups.

There were no significant differences in these parameters among both sex of two groups Tables (1). The data demonstrated that the obese groups, were no significant differences of IL-6, TGF- β1 in both sex of study groups and among three classes of obese groups Tables (1,2) .

Correlation analysis showed that was no significant correlation between BMI with the levels of IL-6, TGF- β1 in obese as well as in sex of the obese groups, Tables (3).

Table (1): The serum concentrations levels of IL-6 and TGF-β1 (pg/ ml) in both sex of study groups

Group / Parameters	Mean ± S.E				P-value of groups
	Control	Obese	Control	Obese	
	Male n=19	Male n=13	Female n=18	Female n=39	
Age(years)	26.85 ± 1.78	23.83 ± 1.22	30.66 ± 1.03	0.13	**0.003***
BMI(Kg/M^2)	34.76 ± 0.79	22.30 ± 1.77	36.23 ± 0.72	0.39	**0.001***
WC (cm)	107.23 ± 3.74	76.77 ± 1.76	108.72 ± 2.25	0.07	**0.001***
Interleukin6(pg / ml)	24.70 ± 1.22	24.49 ± 1.27	23.10 ± 1.10	25.65 ± 1.34	0.21
Transforming growth factor β1(pg/ml)	465.43 ± 37.76	628.44 ± 64.84	541 63. ± 22.97	593.49 ± 28.22	0.10

t-test. *P ≤ 0 .05. S.E: Standard error

Table (2): The serum concentrations levels of cytokines IL-6 and TGF-β1 in obese groups at the three classes of obese groups

Group / Parameters	Obese group (Mean ± S.E)			P-value of groups
	Class I n= 24	Class II n= 17	Class III n= 11	
Interleukin-6(pg/ ml)	26.57 ± 1.51	24.86 ± 2.16	23.49 ± 1.70	0.52
Transforming growth factor-β1(pg/ml	585.24 ± 40.91	606.10 ± 47.94	633.31 ± 50.58	0.79

F-test

*P ≤ 0 .05.

S.E: Standard error.

Table (3): Association between BMI and cytokines IL-6 and TGF-β1 in both sex of obese groups

Groups / parameters	BMI (Kg/M^2)			
	Male		Female	
	R	Sig.	R	P-value
Interleukin-6(pg/ ml)	0.34	0.26	-0.21	0.20
Transforming growth factor-β1(pg/ml)	0.44	0.13	0.08	0.63

Correlation coefficient (r)

* Correlation is significant ≤ 0.05 level.

Discussion

The current study was differed with those Roytblat *et al.*(2000)[10] and Pou *et al.* (2007)[11] whom observed elevated IL-6 levels in fat groups but, data regarding the relevance of IL-6 are discussed this could be partially attributable to the complex etiology of obesity, consisting of the interaction of genetics, diet, and physical activity levels, additionally influenced

by ecological, socioeconomic, and behavioral factors. Where IL-6 exerts many effects, ranging from defense against inflammation and tissue damage and circulating levels of IL-6 correlates with BMI, insulin resistance, and intolerance to carbohydrates [12].

Similarly, Mitrou *et al*. (2011) [13] observe the circulating levels of IL-6 increase with the development of fat mass, and in morbid obesity have been found increased as compared with the non-obese subjects. Meantime increased plasma level of IL-6 is associated with decreased muscular mass or decreased muscle activity . In adding Shahram and Yahya, (2014) [14] exhibited that no significant difference in fasting levels of IL-6 between obese and normal weight men; this discovery relatively proposes that obesity does not affect the level of IL-6.

The recent study prove that the level of IL-6 in the class I more than from class II or class III at the three class of obese groups this is may be due to the different in distribution percentages of class obesity, where class III the least percentage with relatively small size of the sample, or due to IL-6 secretion associated with obesity as a regulatory mechanism attempting to correct excess body weight and achieve negative energy balance, as theorized for obesity-related rises in leptin [5]. Also, may be physical activity daily in the obese groups was not variation than control groups, where high physical activity levels result in low basal IL-6 levels while high basal IL-6 levels escorted low levels of physical activity [15].

The TGF- β1 is a multifunctional cytokine produced by a diversity of cells that is capable of regulating the growth and differentiation of numerous cell types, and this result differed with Yingsong *et al*. (2009)[16] who founded that serum TGF-β1 levels increased with increasing BMI in both male and female ,possibly reflecting physiologically increased TGF-β1 production corresponding to increased fat mass, as commonly seen with leptin and other adipokines ,where the high levels of TGF- β1 in obese animal models could also reflect an important early role in supporting the undifferentiated population in a calorie-rich environment, but also in controlling next differentiation [17].

The level of TGF-β1 in the class III was higher than in class I or class II of obese groups, thus approve with Yadav *et al*. (2011) [18] and Tan *et al*. (2012) where concluded that the TGF-β1 levels on adipose tissue is strongly associated with class III obesity, While the association showed no significant correlation between BMI and TGF-β1 in both groups and both sex of the both groups this may be related to different delivery of the study population in the classes of obese groups, and may be the level of TGF-β1 affected through small size of fat mass.

In addition, the population in this study do not suffer from any chronic disease, where, several lines of evidence were available to support a positive association between TGF-β1 and

obesity which related to disorders. This agree with Torun *et al*. (2007) [19] who observed a positive association between BMI and serum TGF-β1 concentrations in patients with essential hypertension obesity. In addition, Porreca *et al*. (2000) [20] reported that TGF-β1 levels were significantly elevated in hypertensive obese patients compared with hypertensive patients with normal BMI.

Furthermore, in adipose tissue from both obese mice and humans, the levels of tissue TGF-β1 have been shown to correlate well with BMI [21]. Also, there is an association between TGF-β1 polymorphism and both BMI and abdominal obesity was observed in Swedish men [22] . Thus the increased expression of TGF- β1 in the obese adipose tissue may increase adipocyte precursor cell proliferation, thus contributing to the elevated cellularity of fat depots related to the fat phenotype.

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