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Estimation Cut-off values for ST2 , IGF-1 and GALP in obesity

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Abstract: (1) Introductions; Universal, Obesity is a leading cause of preventable chronic diseases. Both obesity and overweight have increased dramatically in recent years. The liver cells mainly secrete insulin-like growth factor-1 (IGF1), which is an anabolic hormone, and its production and release by the pituitary gland are depending on growth hormone. The soluble interleukin-1 receptor is suppression of tumorigenicity-2 (ST2) that was previously known as the interleukin-1 receptor-like receptor1. A neuropeptide known as galanin-like peptide (GALP) is taking part in the control of energy balance. **(2);** Materials and methods: The ST2 levels were carried out by using Afias 10 instrument, IGF-1 by Maglumi 800, GALP by Eliza kit, and data Analysis by XLSTATE program. **(3)** Results; Increase ($p<0.002$, $p<0.001$) the level of ST2 in the overweight comparing to normal-weight, and in obese comparing to normal and overweight groups, and a high AUC (0.85) implies a strong correlation between obesity and the ST2 (ng/ml). Decrease ($P<0.001$, $P<0.0013$) the level of IGF-1 (ng/ml) in obese group comparing to normal and overweight groups, a strong substantial relation between obesity and IGF-1 (ng/ml) is shown by a high AUC (0.92). Increase ($P<0.003$, $P<0.001$) the level of GALP (pg/ml) in obese group comparing to normal and overweight groups, a strong substantial relation between obesity and GALP (pg/ml) is shown by a high AUC (0.88). (4);Conclusions: The relationships between ST2, IGF-1, GALP and obesity are close and fundamental. This may be because the accumulated adipose tissue acts as an inflammatory factor that negatively affect.

keywords: Cut-off values , ST2 , IGF-1 , GALP, obesity.

1 Introduction

Universal, Obesity is a leading cause of preventable chronic diseases. Both obesity and overweight have increased dramatically in recent years. Obesity is associated with and is a risk factor for many diseases such as hypertension, dyslipidaemias, impaired insulin sensitivity/insulin resistance (IR) that leading to type 2 diabetes, non-alcoholic fatty liver disease (extra fats liver), heart disorders, strokes, and tumors, ultimately leading to increased morbidity and mortality rates [1],[2].The liver cells mainly secrete insulin-like growth factor-1 (IGF1), which is an anabolic hormone, that biosynthesis and release by the pituitary gland are depending on growth hormone (GH).This relationship forms the GH-IGF-1 axis, plays a role in metabolism (both carbohydrates and lipids) , body composition, and the development of malignant tumor [3], controlling processes such as cell proliferative, cells differentiate, and cell death, and, in addition, tissue growth and organs functions are affected. IGF-1 is less sensitive to factors that alter GH concentrations than growth hormone because its half-life is longer than that of growth hormone. These factors include exercise, severe dietary restriction, pulsatile secretion, circadian rhythms, and blood sugar changes [4]. IGF-1 is regulated by a number of variables, including dietary consumption (nutritional), hormone levels (cortisol, thyroxine & estrogen). Apart from these physiological control (regulators), IGF-1 levels are

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also influenced by age, disorders that change the concentration of IGFBP, and variations in IGF-1 sampling [5]. The maintaining of normal insulin response, increasing glucose absorption, lowering plasma triacylglycerol, and managing cholesterol are the main metabolic actions of IGF-1. Furthermore, Hepatic glucose metabolism directly increased the transcription of the IGF-1 gene. IGF-1 is affected by a complex of genetic and epigenetic mechanisms in both healthy and pathological cases [6].The soluble interleukin-1 receptor (IL-1R) is suppression of tumorigenicity-2 (ST2) that was previously called as the interleukin-1 receptor-like receptor 1. There are two main types of receptors in serum: the transmembrane and the abbreviated soluble receptors. The soluble interleukin-1 receptor considered an important and novel biomarker of heart stress, fibrotic scarring, and inflammation. Furthermore, the recommendations allow the use of the ST2 as a risk stratification measure and monitoring for patients with heart and cardiovascular diseases [7-9]. A neuropeptide known as galanin-like peptide (GALP) is participating in the control of energy balance. However, GALP appears to have a variety of effects on food consumption and body weight. A neuropeptide GALP, contains 60 amino acids,positions 9–21 of the GALP sequence are homologous to that of galanin. There are a small number of cells that express GALP, most of which are located in the pituitary and hypothalamus glands [10-12].

1. <u>Materials and methods</u>

Ninety sampling their ages (33 to 35) years were used,. Samples have been divided in to:- GROUP1= (30) normal-weight (N.WT)their BMI was (22-24.7 kg/m^2), GROUP2= (30) overweight (O.WT) their BMI was (25.3-29.8 kg/m2) and GROUP3=30 obese (OB) their BMI was (30.4-35 kg/m^2). The ST2 levels were carried out by using Afias 10 instrument, IGF-1 by Maglumi 800, GALP by Eliza kit, and data Analysis by XLSTATE program.

2. <u>Results & Discussion</u>

2.1 Suppression of tumorigenicity-2

The (mean ± SD) of ST2 ng/ml of groups (N.WT, O.WT and OB) levels in the serum were shown in table and figure (1). The results showed increase (p<0.002, p<0.001) the level of ST2 in the overweight comparing to normal-weight, and in obese comparing to normal and overweight groups.

Table (1): ST2 levels

ST2 ng/ml		
N.WT **BMI (22-24.7 kg/m^2)** **n=30**	**O.WT** **BMI (25.3-29.8 kg/m^2)** **n=30**	**OB** **BMI (30.4-35 kg/m^2)** **n=30**
20.3 ± 3.4	23.9 ± 5.6	33.3 ± 3.4
P value		
N.WT/ O.WT	N.WT/OB	O.WT/OB
<0.05	<0.002	<0.001

N.WT= Normal-Weight / O.WT=Overweight / OB=Obese

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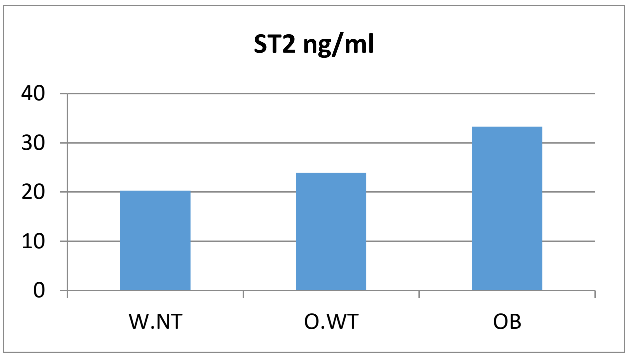

Fig. (1): ST2 levels

Current research examined several biochemical diagnoses for the distribution or illness and determined the best limit or threshold using Receiver Operating Characteristics (ROC) curves. The ROC curve was summarized using the Area under the Curve (AUC). Sensitivity (0.78), specificity (0.95), accuracy(0.81), and ST2 cut-off point (27.9 ng/ml) are provided in table (2). A high AUC (0.85) implies a strong correlation between obesity and the ST2 (ng/ml).

Table (2): Diagnostic properties value of ST2

Sensitivity	**Specificity**	**Accuracy**	**AUC**	**CUT OFF**
0.87	0.95	0.81	0.85	27.9

In chronic inflammatory diseases, a poor prognosis was indicated by high levels of the ST2 marker. Higher concentrations of ST2 and its ligand, interleukin (IL)-33, are found in adipose tissue in obese patients [13]. Zeyda et al. reported that obese individuals had higher levels of sST2 in plasma compared to lean or non-obese controls, as well as increased expression of ST2 and IL-33 in adipose and subcutaneous tissue [14]. In addition, Gleimer et al found that among adolescents and adults, obese individuals had greater sST2 than normal-weight patients [15] .Oxidative stress and inflammatory markers were positively associated with elevated circulating sST2 levels in metabolic syndrome patients [16]. Numerous clinical and experimental findings imply that : sST2 has a role in inflammatory illnesses [17]. Obese animals have higher levels of sST2, which is reflected in elevated markers of vascular inflammation[18]. Furthermore, associations between inflammatory markers and sST2 have been reported in a number of illnesses [19-20]. The proinflammatory compounds linked to raised sST2 levels have the capacity to stimulate and activate inflammatory cells in injured blood vessels, making them particularly crucial as a risk factor for metabolic syndrome, and they are essential for the onset and development of insulin resistance and inflammation in adipose tissue [21-22].

2.2 Insulin-like growth factor-1

The (mean ± SD) of IGF-1 ng/ml levels in (N.WT, O.WT and OB) groups were listed in table (3) and in figure (3). The results found decrease (P<0.001, P<0.0013) the level of IGF-1 (ng/ml) in obese group comparing to normal and overweight groups.

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Table (3): IGF1 levels

IGF-1 ng/ml		
N.WT BMI (22-24.7 kg/m^2) n=30	**O.WT BMI (25.3-29.8 kg/m^2) n=30**	**OB BMI (30.4-35 kg/m^2) n=30**
178.8±45.6	167.7±39.1	95.3±22.2
P value		
N.WT/ O.WT	N.WT/OB	O.WT/OB
≥ 0.05	<0.001	<0.0013

N.WT= Normal-Weight / O.WT=Overweight / OB=Obese

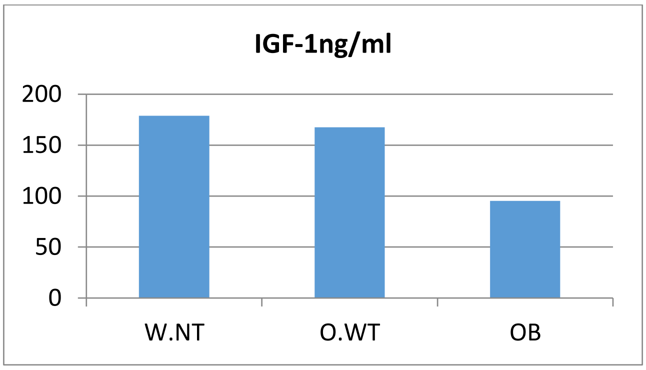

Fig. (2): IGF1 levels

Sensitivity(0.90), specificity(0.88), accuracy(0.83), and IGF-1 cut-off point (136.90ng/ml) are provided in table (4). A substantial relation between obesity and IGF-1 (ng/ml) is shown by a high AUC (0.92).

Table (4): Diagnostic properties of IGF1

Sensitivity	Specificity	Accuracy	AUC	CUT OFF
0.90	0.88	0.83	0.92	136.90

There are several limitations to this study. First, the fact that the samples were collected from a single hospital and a single external laboratory and the small sample size reduces statistical power. Several studies have shown that IGF-1 and BMI have a negative relationship [23-25], despite contradicting findings, it has also been observed that obese people have normal or high IGF-1 levels. There is strong evidence linking the pathophysiology of obesity to the growth hormone/insulin-like growth factor system. Adipose tissue and the pituitary gland interact through the mechanism of this system, which is directly influenced by growth hormone and insulin-like growth factor on the growth and division of fat cells [26]. Additionally, they disclosed the manifestations of obese individuals with low IGF-1, including heightened inflammation and adiposity as well as metabolic comorbidities such hyperuricemia . Furthermore, in individuals without diabetes, low IGF-1 levels were linked to increased blood glucose in people with higher BMI [27-29]. Unlike our findings, De Marinis et al. observed that IGF-1 did not substantially change in obese female patients before and after weight loss [30]. Utz et al. reported that IGF-I levels were not significantly decreased [31]. Additionally, the results conflict with those of other studies that have found that: Hyperinsulinemia induced by insulin resistance reducing circulating binding protein and raising free levels of IGF-1 in the blood [32-37] .

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2.3 Galanin-like peptide

The (mean ± SD) of GALP pg/ml levels in serum of (N.WT, O.WT and OB) groups were listed in table (5) and in figure (3). The results found increase (*P*<0.003, P<0.001) the level of GALP (pg/ml) in obese group comparing to normal and overweight groups.

Table (5): GALP (pg/ml) levels

GALP pg/ml		
N.WT **BMI (22-24.7 kg/m^2)** **n=30**	**O.WT** **BMI (25.3-29.8 kg/m^2)** **n=30**	**OB** **BMI (30.4-35 kg/m^2)** **n=30**
396.39±88.20	422.12±78.91	513.36±110.01
P value		
N.WT/ O.WT	N.WT/OB	O.WT/OB
≥ 0.05	<0.003	<0.001

N.WT= Normal-Weight / O.WT=Overweight / OB=Obese

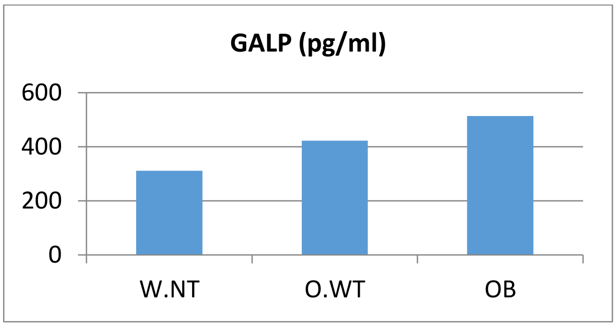

FIG. (3): GALP (pg/ml) levels

Sensitivity(0.94), specificity(0.89), accuracy(0.81), and GALP cut-off point (449.31pg/ml) are provided in table (6). A strong substantial relation between obesity and GALP (pg/ml) is shown by a high AUC (0.88).

Table (6): Diagnostic properties value of GALP

Sensitivity	Specificity	Accuracy	AUC	CUT OFF
0.94	0.89	0.81	0.88	449.31

Galanin has a variety of central and peripheral effects. It is specifically linked to endocrine processes that regulate anterior pituitary hormone, reproduction, carbohydrate metabolism, inflammation, appetite, obesity gain, impaired insulin sensitivity, hypertension, and overall metabolism [38]. Human studies have demonstrated the contribution of GAL in metabolic diseases. Patients with gestational diabetes and high BMI have significantly higher plasma GAL levels [39–41]. Since GAL is associated with increased food intake, functional characterization so far has shown that it acts primarily as an appetite stimulant [42], and Weight has an impact on the body's levels of galanin [43]. results concur with the study's finding that obese patients have greater blood galanin levels [44]. Elevated blood levels of galanin in obese individuals may be due to being overweight or may be one of several variables and risk that contribute to obesity [45].

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3. **Conclusions**: Obesity has a clear effect on the studied variables (ST2, IGF-1, GALP) , whose levels in serum were changed significantly. This may be because the accumulated adipose tissue acts as an inflammatory factor that negatively affect.

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