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Irisin biomarker, TSH, Trygleceriads and High Density Lipoproteins in thyroid diesase patients

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Introduction:

Thyroid hormones stimulate protein synthesis and increase the rate at which triglycerides are broken down (lipolysis)and that is why they are sometimes taken by athletes in sports where physical appearance is judged, especially during the final stages of pre-contest dieting, because at appropriate time level,these hormones help preserve muscle and reduce body fat, but when used incorrectly or excessively ,they are highly destructive to muscle .The thyroid secretes about ten times T4 as much asT3;although,T3 is roughly two to three times more potent than (T4) which is converted into the more active triiodothyronine with the selenium –dependent enzyme 5-deiodinase.T3 and T4 are lipid soluble and combine with special transport proteins upon release into the blood serum called thyroxin –binding globulins (TBG), and less than one percent of thyroid hormones travel unattached in their free state. During growth ,thyroid hormones provide an anabolic influence on protein metabolism due to their influence on insulin secretion.T4 and insulin also connect in liver ,where they mutually affect insulin growth factors (IGF) which are powerful muscle building control agents and in the absence of adequate levels of thyroid hormones ,human growth hormone (hGH)also loses its growth –promoting action and is not secreted normally[1]. T3 is recognized as a key metabolic hormone of the body. Which has many physiological actions and it modulates all metabolic pathways through alterations in oxygen consumption and changes in protein,lipid,carbohydrate, and vitamin metabolism. Through its direct manipulation and degradation of many other hormones and growth factors it indirectly influences additional endocrine signaling. Abnormalities of the thyroid function are among the most common of the endocrine disorders .They fall into two categories , hypothyroidism and hyperthyroidism , reflecting deficient and excess thyroid hormone secretion. There are many causes that generate these conditions and whatever the causes, the consequences of too little or too much thyroid hormone secretion are largely predictable hormones[2].

Irisin, is a myokine whose levels seem to increase during physical exercise leading to heat generation and a possible protective effect on metabolic disorders[3]. Irisin seems to induce a brown –like phenotype in some white adipocytes, which improves multiple metabolic parameters by increasing energy expenditure[4]. Therefore, irisin could play a hypothetical protective role against different conditions ,such as cardiovascular diseases , type 2 diabetes mellitus (T2DM) or fatty liver disease .Moreover , through the improvement of obesity and its associated chronic inflammatory state, irisin may have a potential role in obesity–related cancer prevention as well as in osteoporosis and neurodegenerative diseases[5].HoweverWu*et. al.,* 2012[6]reported that only part of the subcutaneous adipose tissue inverts into brown adipose tissue (BAT), with a substantial portion dose not demonstrate features consistent with classical white adipose tissue (WAT) or BAT which they refer to it was beige adipose tissues.These beige fat cells have been shown to be a cell type distinct from white or brown fat cells being located in white adipose tissue[3,6].Besides its occurrence in skeletal muscle, irisin was detected – although in much smaller quantities – in several human tissues containing smooth muscle as well as heart

muscle, and organs including liver, kidney, and lung[7] .Although its relationship with many diseases, such as type 2 *diabetes mellitus*, metabolic syndrome, insulin resistance, chronic renal disease, and anorexia nervosa has been investigated, its association with the thyroid functions tests (TFT), in patients with thyroid diseases remain unknown.

As reported by Zhang[8], plasma irisin level seems to correlate negatively with intrahepatic triglycerides content, being significantly reduced in obese Chinese patients with Non-Alcoholic Fatty Disease (NAFLD). In patients with chronic renal failure, there is an inverse relationship between irisin and High Density Lipoprotein (HDL).HDL cholesterol protects against atherosclerosis by its inhibitory effect on cholesterol transport and anti-inflammatory effect[9].HDL cholesterol is a clear predictor of vascular events in the overall population[10].The inverse relationship between intrahepatic triglyceride level and irisin and the potential direct relationship between irisin and HDL reinforces the potential protective role of irisin, especially in patients with a chronic disease of high cardiovascular risk, such as fatty liver disease. These findings warrant further study of the potential role of irisin in the metabolism of HDL cholesterol[11].

Materials & Methods

A hundred subjects (60 females &40 males) ranged 12-70 years of age were used for this study.The60 females included 34 patients and 26 healthy subjects served as control.The 40 males were 24 patients and 16 healthy subjects used as control. Sera were collected from patients and healthy subjects referred to Teaching Laboratories in AL-Hilla teaching hospital and from private laboratories (Babylon), during the period from November 2015 to March 2016. Least significant Difference(LSD) test, correlation coefficient were used to analyze the results.

Thyrotropin (TSH), determination.

Elisa Kit supplied by ACCU Bind Elisa Microwlls, MonobindInc., USA was used for the determination of TSH.

Irisin, Triglycerides & High Density Lipoprotein (HDL).

Elisa Kit, supplied by Elabscience was used for FNDC5 measurement, Triglycerides and HDL were measured by using(REFLOTRON PLUS analyzer) from Roche company (GERMANY).Thirty-two microliter of serum were put on the stripe of Reflotron kit, and the results were given after few minutes.

Results

Thyroid stimulating hormone (TSH) levels and Irisin hormone were measured in sera of the control and patients hypothyroid and hyperthyroid males & females patients.

The results showed that Irisin level stable (1) was higher in hypothyroid females than control and was lower in hyperthyroid females than in control and was higher in hypothyroid males than in control and was lower in hyperthyroid males than in control .

The TSH level was higher in hypothyroid females than in control and was lower in hyperthyroid females than in control, and was higher in hypothyroid males thanin control and was lower in hyperthyroidmales than incontrol.

Triglyceride level was higher in hypothyroid females than in control and was lower in hyperthyroid females than in control and was higher in hypothyroid males than control and was lower in hyperthyroid males than in control .

HDL level was lower in hypothyroid females than in control and was higher in hyperthyroid females than control but was higher in hyperthyroid males than control and lower in hypothyroid males than control. As to the correlation between Irisin & HDL, there was a significant positive correlation, whereas that between Irisin and TSH was significantly positive and that between TG and Irisin was significantly positive.

Table (1)comparison between female's patient andmales' patients

	females			Males		
parameters	**Normal**	**Hypothyroid**	**Hyperthyroid**	**Normal**	**Hypothyroid**	**Hyperthyroid**
Irisin(ng/ mL) level	1.60±0.56 b	3.98±0.94 c	0.78±0.45 a	1.70±0.61 b	3.68±0.65 c	0.78±0.48 a
TSH(mLU/L) level	1.25±0.58 b	12.27±3.56 c	0.25±0.08 a	1.28±0.65 a	13.71±4.35 b	0.24±0.05 A
TG(mg/dL)level	70.69±1.7 b	83.40±4.04 c	55.10±6.06 a	71.38±2.1 b	82.40±4.70 c	56.08±5.47 a
HDL(mg/dL)level	22.86±1.3 b	18.60±1.15 a	31.29±2.03 c	21.61±0.9 b	18.22±1.24 a	30.14±1.96 c

Different letters indicate significant differences between

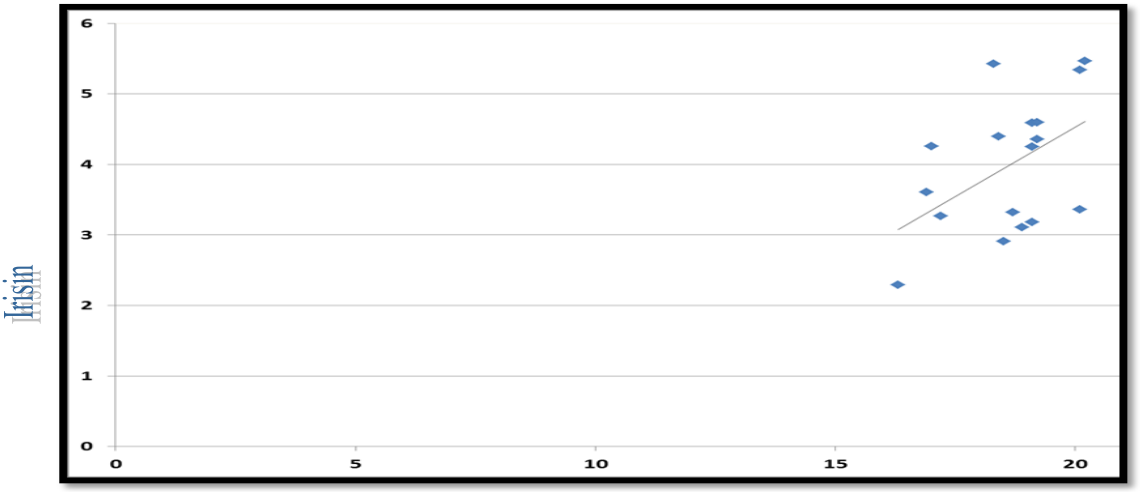

Figure (1)positive significant correlation between HDL and Irisin

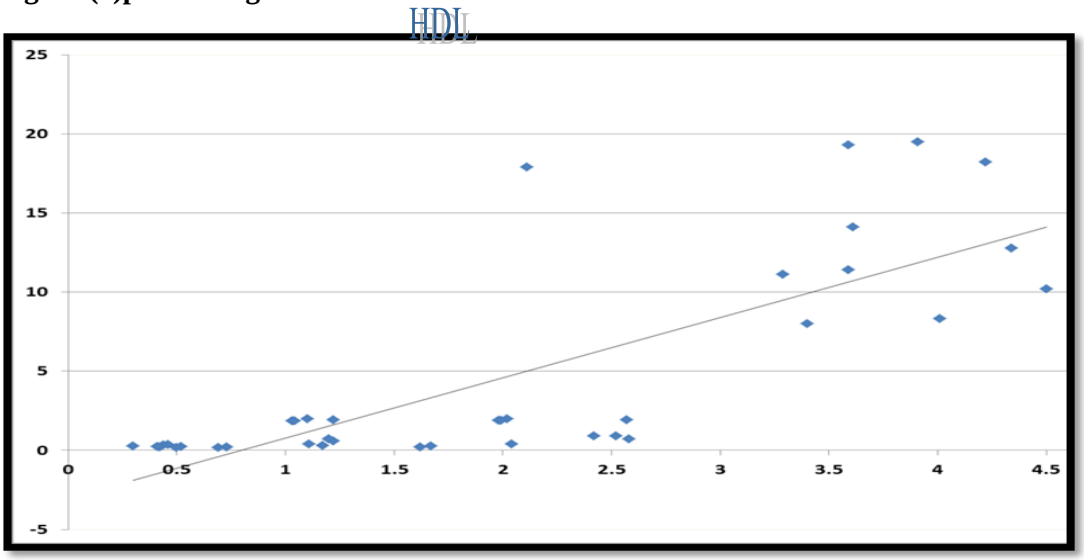

Figure (2) positive significant correlation between Irisin and TSH

Discussion

Irisin is a myokine whose levels seem to increase during physical exercise leading to heat generation and a possible protective effect on metabolic disorders[3] .Irisin seems to induce abrown-like phenotype in some white adipocytes which improves multiple metabolic parameters by increasing energy expenditure[4].The results of Irisin obtained from this study are in agreement with our previous work who found that serum irisin levels

were higher in hypothyroid group compared to control group. Irisin is a newly discovered adipo-myokin, which is reported to have a significant influence on the body metabolism and thermogenesis .Other influencing factors on metabolic state are thyroid hormones, which increase heat production and control the energy balance. Due to numerous similarities in action it seems imperative to explore this substance potential mutual influence on the body.

TSH levels increase in hypothyroidism causes the differentiation of preadiposcytes which become adipocytes that has been used in the most intensively studied models of cellular differentiation[12].The lower levels of TSH in hyperthyroidism patients are in agreement with[13].

HDL level in hypothyroid patients was significantly lower than in healthy subjects and was significantly higher in hyperthyroid patients than normal. This result is in disagreement with[14] on hyperthyroid patients .Thyroid hormones can influence HDL metabolism by increasing cholesteryl ester transfer protein (CETP) activity,which converts HDL2 to the low density lipoproteins (VLDL) and TGs to the opposite direction[15].

TG level was significantly high in hypothyroid patients than control and was significantly lower in hyperthyroid patients than controls, a result may be related to cardiovascular disease resulted from the increase of thyroid hormonesin hypothyroidism and hyperthyroidism respectively and may also be explainedby the decrease of weight in hyperthyroidism patients. These results agree with[14,16,17] who indicated that hyperthyroidism was associated with decreased levels of lipoprotein, caused by increased hepatic uptake due to an enhanced affinity for the Low Density Lipoprotein (LDL) receptors, and regulatory protein of TG(ApoAV).

Conclusion:

TG level was significantly high in hypothyroid patients than control and was significantly lower in hyperthyroid patients than controls, a result may be related to cardiovascular disease resulted from the increase of thyroid hormones in hypothyroidism and hyperthyroidism respectively and may also be explained by the decrease of weight in hyperthyroidism patients**.**

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