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Association of Irisin concentration with clinical Parameters in Obesity patient compared with sport individual in Iraqi population

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Abstract:

Introduction obesity is a complex disorder has an impact on morbidity and mortality with genetic factors, and is an accumulation of excess fat in adipose tissue where conceder risk factor for a variety of chronic medical condition with a major negative impact on human health, the previous 30year, Irisin, the novel myokine secreted as a product of fibronectin type III domain containing 5 protein (FNDC5), is a newly recognized peptidicmyokine, Irisin is regulated by response to (PGC1)-α peroxisome proliferator-activated receptor coactivator-1-α activation.

Methodology A case–control study included 177 individuals ((129) obese patients with Obesity and (59) sport control). Plasma irisin and insulin concentrations were measured with (ELISA) kit (Elabscience Com. USA). The assay has been proven highly sensitive to human irisin. The sensitivity of the assay was 0.2 ng/mL, and the linear range of the standard was 1 to 1000 ng/mL, glucose, triglycerides, and total cholesterol, HDL, and LDL were determined in serum with the use of clinical-grade reagents from Pointe Scientific, supply by Biolabo Company and following the manufacturer's instructions.

Result: the comparison of obese patients with sport control the result demonstrated all anthropometric and metabolism parameters significance difference Age (P<0.001), BMI (P<0.001), WHR (P<0.001),Systolic (P<0.001), diastolic (P<0.001), FBG(P0.007), TG (P<0.001), TC (P<0.001), HDL-C (P<0.001), VLDL (P<0.001), LDL (P<0.001), HbA1c (P<0.001), insulin (P<0.001), HOMA IR (P<0.001), Irisin (P<0.001).

Conclusion: Increase of irisin level leads to elevated of energy expenditure by activation of browning process and enhancement of insulin resistance and regulated of glycemic indices. circulation of the irisin levels between sport and obese patients.

Key word: Irisin; exercise; Obesity; FNDC5.

INTRODUCTION:

Obesity is defined as a complex disorder has an effect on mortality and morbidity with strong genetic components and is a complex deposit of excess large content in adipose tissue (Ahima 2011; Aljawadi 2013) and conceder a risk factor for a multiplicity of chronic disease condition with a bad impact on health of human. Over the previous 30year, increasing dramatically in worldwide (Wang *et al.* 2008). With twice, amplifying rates for childhood and adult obesity and teenager obesity triplicating rates (12–19 years), (Upadhyay *et al.* 2018).

The Prevalence of obesity and overweight increased by 27.5% in the adult's population and 47.1% in the children among 1980 and 2013 in the Worldwide. Recently WHO international evaluations follow.

The Bostrom *et al.* improve reported the expression of PGC1α in muscle activation the improved of FNDC5 expression.(Panati, Suneetha, and Narala 2016) The function of FNDC5 as a receptor has not been explore. Secretion of soluble irisin to extracellular after cleavage linking peptide (Bostrom *et al.* 2012). Indeed, since its detection, several research have focused on the functional role of irisin (portion of a polypeptide on a cell membrane that extends beyond the membrane into the extracellular space) in metabolism (Moon, Dincer, and Mantzoros 2013; Roca-Rivada *et al.* 2013; Stengel *et al.* 2013).

Irisin, a novel polypeptide hormone, is proteolytically processes from (FNDC5) fibronectin type. III domain containing protein 5 (Liu *et al.* 2017), which is highly expressed in heart and skeletal muscle, (Kozakova *et al.* 2013). previous studies showed FNDC5 was also expressed in other tissues, such as adipose tis- sue and liver, which indicates additional functions of this hormone (Roca-Rivada *et al.* 2013; Chen *et al.* 2016; Gizaw, Anandakumar, and Debela 2017)

The rise amount production of uncoupling protein1(UCP1) due to in the relatively low in WAT rate in BAT, while its expression can be high metabolic (Spiegelman 2013; Chen *et al.* 2016), However, Synthesis and release of Irisin are prompted by exercise and peroxisome proliferator-activated receptor-γ (PPAR-γ) co-activator 1-α (PGC1α) (Christensen *et al.* 2011). Previous indication has a series of uncertainties associated with the biological functions of irisin in human (Raschke *et al.* 2013; Timmons *et al.* 2012). Irisin is assumed to play a part important in metabolism, sugar and fatty acid homeostasis, cardiac and endothelial roles and in the CNS (Wang and Pan 2016; Efe *et al.* 2017; Tekin *et al.* 2017). There are numerous factors were found have affected the physiological levels of irisin in the body such as exercise, diet, obesity, and different pharmacological reasons. (Mahgoub *et al.* 2018).

Exercise with irisin:

Exercise is the first mark of therapy for numerous metabolic diseases such as diabetic and obesity, but also progresses outcomes in diseases involving other peripheral tissues, such as the heart, liver and brain.(Jedry *et al.* 2015) Exercise is identified to induce weight loss, which is more than probable due to energy expenditure during exercise, and Physical exercise aids a variety of organ systems in living thing including insulin sensitivity and obesity.as well

as illustrated in (figure1.7). However**,** Many revisions have highlighted the role of exercise in several body part systems as a liver, adipose tissue, brain, and heart. The exercise affects the skeletal muscle directly between all other organs (Pedersen and Febbraio 2012; Panati *et al.* 2016).

There are More than one thousand genes are stimulated in skeletal muscle response to exercise and donate to improved health (Keller *et al.* 2011; Pedersen and Febbraio 2012; Thompson *et al.* 2012). Indeed, deficiency of exercise is a major reason of chronic diseases like muscle aging, obesity, metabolic syndrome, insulin resistance, pre-diabetes, Type 2 diabetic, etc. Skeletal muscle has the capability to express many myokines (Schumacher *et al.* 2013) The skeletal muscle is a metabolically energetic tissue that has been recognized as a secretary organ since it products and releases cytokines and other peptides like to hormones in function these biomolecules might be involved in the of assistance effects of exercise. Some of myokines that secretion by the skeletal muscle consist of IL-15, IL-8, IL-6, irisin, leukemia inhibitory factor, fibroblast growth factor (Pinto *et al.* 2012; Panati *et al.* 2016).

Exercise, Diet, and weight wegulator in human given that people are at risk for increase of weight and obesity, (MacDonald 2012) Exercise promote PGC-1α expression in adipose tissue, and muscle, which is assuming to intermediate several of its health aids. The PGC-1α are suggested regulate muscle secretion factors with special effected on energy expenditure. On the other hand.(Andreia Cunha 2012).

In an previous study, the writers suggested the name of 'myokines' for the secretions of skeletal muscle which work as endocrine, autocrine or paracrine and "Adipokines" for the secretion of adipose tissue mechanisms that showed in figure(1.8) (Panati *et al.* 2016)

Irisin, is a myokine stimulated by exercise (Anastasilakis *et al.* 2014) which encourages "browning"(is a converted the white adipose tissue to brawn fat process) of adipose tissue and thermogenesis,Where the Irisin proteolytic product from the fibronectin type III domain containing 5 (FNDC5) that is a trans membrane protein, whose expression it by induced the peroxisome proliferator-activated receptor (PPAR)-γ co-activator 1α (PGC-1α).

The promising mechanism of irisin for stimulation of beige adipocytes, numerous studies have been stated on the effects of irisin in both in vivo and in vitro and showed to increase Serum irisin levels after exercise (Aydin *et al.* 2014).

Irisin is assumed to preventable obesity by increasing the expression of mitochondrial (UCP1) uncoupling protein1 and stimulated the browning fat, the process done (WAT) with white adipose tissue secures brown-like properties. These brown identical adipocytes are named beige fat cells and are also involved in thermogenesis(Novelle *et al.* 2013; Roberts *et al.* 2013; Hofmann, *et al.* 2014; Mahgoub *et al.* 2018) Some study referred to the elevated irisin level with exercise up to 2-fold compared to the no exercised in humans, which suggest that irisin is existing in the plasma and upturn with exercise (Bluher *et al.* 2014).

In the first description of this hormone, increased levels of circulating irisin were associated with improved glucose homeostasis by reducing insulin resistance. (Gizaw *et al.* 2017) Irisin increases the total energy expenditure, prolongs life expectancy, participate in the loss of body weight, and decrease of insulin resistance, thus reducing obesity and insulin resistance.(Sanchis-Gomar and Perez-Quilis 2013) .

More interestingly, it has been recently demonstrated that irisin is not only a myokine but also an adipokine (Rivada *et al.* 2013). Given the against of obesity and antidiabetic properties of brown fat formation the 100% homology between human and murine irisin, this hormone seems to display great healing possible in these and associated disorders. PGC-1α in muscle encourages the release into the circulation of a newly recognized hormone, irisin, which shows regulatory effects on adipose tissue, a study in Nature reveals. (Cunha 2012).

MATERIAL AND METHODS:

A case–control study included 177 individuals ((129) obese patients with Obesity and (59) sport control).

The study data were collected as a Completed questionnaires which measures Physical examination was done by take the height, weight, to calculate BMI and take the waist, Hip to determine the waste ratio in four categories (normal weight, overweight, moderately obese, and obese) (Doll, Petersen, and L. 2000) and blood pressure measured. The obese at Al-Sadder Medical City, Al-Najaf, Iraq.

Measurement anthropometry and physical activity:

Body mass index value obtained according to the following equation (Eknoyan, 2008) BMI = Weight (kg)/Height (m^2). Electronic balance was used to measure the weight and height of the Participants. The subjects were Consider as obese when the BMI (30 kg/m2) and overweight when BMI (25-29 kg/m2) and normal when BMI ranged (18.5-24.9kg/m2) (Guyton & Hall, 2006).

Waist circumference was measured in centimeters via tape measure at the widest point between the lower border of the right costal margin and the top of the iliac crest. Hip circumference was measured at the widest point of the hips and buttocks. Waist to hip ratio (WHR) was measured by simple division of waist on hip measurements.

Collection of blood and assay procedure:

After 12 hours overnight fasting, 6 ml of venous blood were withdrawn from every individual by sterile syringe and divided into three tubes:

- Tow ml of blood were transported into EDTA tube was used for quantitative colorimetric determination of glycated hemoglobin (HbA1c) using diagnostic kits.
- The another 2ml of whole blood were collected in gel tube without anticoagulants after that, was left for (10-15min) to allow clotting formation and then centrifuged at 4000 rpm for 10 minutes.

The sera was separated and divided into two ependorff aliquots the first to one the enzymatic colorimetric methods by the spectrophotometric measurement were used for determination of FBS, and lipid profile like (TC, HDL, LDL,TG) and stored at deep freezing (-80 ºC) at the Center

blood bank in Al-najaf Al-Ashraf until time of use. (Abdu Allah *et al.* 2017) The second eppendorf containing remain sera that also stored at deep freeze until biochemical analysis of serum hormone and myokine like (Insulin and Irisin) concentration by ELISA technique. (Papp 2017).

Plasma irisin and insulin concentrations were measured with (ELISA) kit (Elabscience Com. USA). The assay has been proven highly sensitive to human irisin. The sensitivity of the assay was 0.2 ng/mL, and the linear range of the standard was 1 to 1000 ng/mL, glucose, triglycerides, and total cholesterol, HDL, and LDL were determined in serum with the use of clinical-grade reagents from Pointe Scientific, supply by Biolabo Company and following the manufacturer's instructions.

RESULT AND DISSECTION:

The biochemical characteristics of the conscripted individuals were illustrated in table (3.1), the result revealed to significant differences of age (p<0.001), BMI (p<0.001), WHR (p<0.001) were noticed during a comparable among the obese patient with those of the control sport group.

Table 3.1 Basic characteristics of study groups between sport and obese.

Parameter	Control Sport (Mean ±SD)	Obese patient (Mean ±SD)	P-value
Number	59	129	-----
Gender (male/female)	59/0	129/12	<0.001
Age/ year	23.44±4.5	36.57±10.16	<0.001
BMI (kg/m2)	22.62±2.22	32.84±5.14	<0.001
WHR	0.84±0.08	0.96±0.16	<0.001

P-value < *0.05 is significant.* BMI=*body mass index,* WHR= *waist-to-hip ratio*

The population of obese patient has risen and are still rising in development countries. According to "Obesity Update 2017 Report" published by Organization for Economic Cooperation and Development (OECD), as mentioned by (Mehrabani and Ganjifar 2018). According to assessments, more than half of disease related with lifestyle. Indeed, obesity increases the risk of several diseases and health environments with increase of BMI and WHR.

In this study, the association between obesity patient and control sport high associations with Age, BMI and WHR. Overall, showed stronger association with risk of increase obesity through the elevated of BMI and WHR value and this result agreement with lee *et al* 2018. (Lee *et al.* 2018).Body Mass Index, and waist-to-hip ratio (WHR) have also been reported that as high risk factors for cancers such as colon cancer. WHR is a useful method for assessment of central obesity as mentioned by Mehrabani and Ganjifar 2018. (Mehrabani and Ganjifar 2018).

Biochemical data to Comparison of the control sport and obese patients

The result of comparison between the control sport and obese group are listed in table 3.2 where shown the all anthropometric and metabolism parameters of obese subjects are significance compared with the control sport as well as the Age (P<0.001), BMI (P<0.001), WHR (P<0.001),Systolic (P<0.001), diastolic (P<0.001),FBG(P0.007), TG (P<0.001), TC (P<0.001), HDL-C (P<0.001), VLDL (P<0.001), LDL (P<0.001), HbA1c (P<0.001), insulin (P<0.001), HOMA IR (P<0.001), Irisin (P<0.001). Based on previous studies, the decrease physical activity causes decrease age of human for nearly 5–10 years when compared with that of people doing regular physical activity or exercise(Chen *et al.* 2016). In most studies Irisin concentrations increased with exercise (Loffler *et al.* 2015; Norheim *et al.* 2014;Huh *et al.* 2015).

The regular exercise promote generates peptide as one of the myokines in muscle, that will secreted into blood stream and transport to adipose tissue or organs for performing the regulation of energy metabolism, activation of converted with adipocyte to brown adipocyte process , enhancing the activity of insulin and reducing IR, and adjusting the body preparations(Winn *et al.* 2017; *Jorge et al.*2012) Because of its physiological regulation of exercise induced irisin for health promotion and many diseases.

Irisin expression was proportional with increase regular exercise is needed daily living the irisin activated browning of white adipocytes can be achieved through the expression of UCP1 and regulated through the activation of p38 mitogen activated protein kinase (p38 MAPK). The patients with diabetes reveal a lower level of circulating irisin in contrast irisin the obviously improved glucose resistance and mainly acts on WAT and functions as the improved energy consumption, which can reduce high fat diet and reduce insulin resistance (Chen *et al.* 2016; Kim *et al.* 2018).

Table 3.2 Comparison between sport control and obese

Parameter	control Sport (No.59) (Mean ±SD)	Obese (No.129) (Mean ±SD)	P-value
Systolic (mmHg)	12.00±0.14	12.44±1.09	<0.001
Diastolic (mmHg)	7.99±0.14	8.25±0.77	<0.001
FBG(mg/dl)	90.95±16.93	100.29±23.70	0.007
TG (mg/dl)	144.42±51.72	196.39±59.77	<0.001
TC(mg/dl)	186.59±35.54	258.20±88.38	<0.001
HDL-C (mg/dl)	52.49±13.64	75.44±25.74	0.001
VLDL (mg/dl)	28.89±10.35	39.27±11.95	<0.001
LDL (mg/dl)	105.53±33.63	143.93±93.80	<0.001
HbA1c %	5.74±0.95	7.42±1.14	<0.001
Insulin (µIU/ml)	3.3± 2.74	9.11±5.51	<0.001
HOMA-IR	0.74±.64	2.27 ±1.5	<0.001
Irisin (ng/ml)	9.29±2.19	7.76±2.50	<0.001

FBG= *Fasting blood Glucose,* HbA1C= *Hemoglobin A1c,* HOMA-IR =*homeostatic model assessment-insulin resistance, TG= triglyceride,* TC= *total cholesterol,* VLDL= *very low density lipoprotein,* LDL= *low density lipoprotein,* HDL-C= *high density lipoprotein-cholesterol, Irisin= novel myokin.*

This study agreement with several studies (Loffler *et al.* 2015; Kurdiova *et al.* 2014; Fukushima, *et al.* 2016; Amaro Andrade *et al.* 2018) that believed with regular exercise where increase irisin concentrations after periods of exercise. These results indicate that the irisin is a myokine stimulate by exercise, where increase the enhancing of energy expenditure by activation of mitochondrial thermogenesis.

level of serum irisin elevated through exercise, have beneficial effects on muscle function and strength, avoid longer term causes a weakening of muscle (Kim *et al.* 2015). Therefore, the possible irisin increase through exercise uses result a growing and helpful effect on the body health.

In this study convention with other study (Pekkala *et al.* 2013; Aydin *et al.* 2013; Loffler *et al.* 2015).that suggested the irisin level increase was more distinct after exercise such as sport group in this study, than low exercise as well as obese group.

Treatment of obesity by exercise is possible that one of the mechanisms related to this effect may be associated to the rise in irisin thermogenesis and production.(Amaro Andrade *et al.* 2018) the exercise controlled irisin myokine was recognized and defined as a link between bodybuilding and the elevation of WAT browning process. Initially confirmed that the irisin and FNDC5 encourage browning of WAT resulting in the condition of irisin as a therapeutic method in the match beside obesity and its connected to diseases of metabolic, it is vital to show that the irisin has an influence on convert the WAT white adipose tissue to brown in cell of human that contribute in reduce of obesity(Bostrom *et al.* 2012; Elsen, Raschke, and Eckel 2014).

In this study Irisin levels rise after physical activity such as sport group believed with Kim 2018 whereas the irisin level in the obese patient remained without change in adult male and female individual without an exercise interference and that reach a convention with Kim *et al.* 2018(Kim 2018).

subjects have elevated circulation of irisin absorptions presented more of metabolic significant improvement (Fukushima, *et al.* 2016; Norheim *et al.* 2014) and some studies showed the levels of irisin rises recovers glucose homeostasis and energy expenditure like a result Askari *et al.* 2018 (Askari *et al.* 2018) One of the factors, which shows that the elevated in irisin circulating may, contributed in the improvement control of diabetes and insulin resistance. (Amaro *et al.* 2018).

The current results exhibit raised of irisin level and decrease in level of lipid profile, fasting blood glucose and insulin resistance to the sport group compared with the obese group patient, this result indicate the irisin play crucial role in the metabolic activity and energy expenditure. The exercise and elevated of irisin considered beset condition to treatment of obesity and several disease such as metabolic syndrome, diabetic, cardiovascular disease, insulin resistance and hypertension.

Correlation of anthropometric with level of Irisin:

There is non-significant (negative correlation) was detected between the amount of serum Irisin levels and anthropometric characteristics of the obese patient. Where the ($P > 0.05$) of the age, BMI with levels of irisin except the WHR where no correlation with levels of irisin in the serum as well as shown in the table 3.3 and the relationship between the anthropometry value and the irisin level was negatively correlation except WHR where the r value of age, BMI and WHR with irisin (r=-0.117, p0.188), (r=-0.123, p0.165) and(r=-0.003, p0.977) respectively

Table 3.3 correlation of anthropometric with concentration of Irisin level.

Parameters	Values	Irisin Level
Age (year)	r	-0.117
	P-value	0.188
BMI (kg/m^2)	r	-0.123
	P-value	0.165
WHR	r	-0.003
	P-value	0.977

P-value > 0.05 is not significant, r-value lees than 1
BMI= body mass index; WHR = waist to hip ratio.

The relationship between Irisin level and anthropometric characteristics of the obese subjects were evaluated by using Pearson's correlation tests. The Negative correlations were detected between Irisin levels and the anthropometric factors including age, BMI, and waist to hip ratio (WHR).

Other researchers have noticed a negative correlation between irisin concentration and age, suggesting that the lesser muscle mass in the elderly would make release and lower irisin production, then skeletal muscle is the main tissue accountable for its production.(Amaro Andrade *et al.* 2018).

This results revealed to weak negatively correlation between the BMI and irisin because the environmental condition, life style and most reason is the physical inactivity and didn't regular exercise which cased weakness to the skeletal muscle due to decrease activity to secretion of irisin by the muscle where amount of muscle is the main predictor of the serum level of irisin.

Serum irisin levels increase in response regular exercise because it activates the transcriptional co-activator PGC1α in muscles and stimulates the expression of FNDC5 protein, a membrane protein that cleaved and secreted as irisin acts on white adipose cells, which stimulate UCP1 expression and brown fat progress.

Correlation Parameters HbA1c, fasting plasma glucose, Fasting serum Insulin, HOMA Insulin Resistance with Irisin.

The results of correlation irisin circulating level was negative significance with the glucose homeostasis parameters except the fasting blood sugar were positive as presented in the table 3.4.

The values of correlation person's model presented the negative value of irisin with HbA1c (r -0.186, p 0.035), irisin with fasting insulin (r -0.292,p 0.001), and the irisin with HOMA-IR (r -0.230, p 0.009) where the significance deference between them and this result are respectable to the maintenance and controlled the glucose level and preventable diabetic mellitus.

Table 3.4 Correlation glucose homeostasis with irisin

Parameters	value	Irisin level
FBG (mg/dl)	r	0.102
	P	0.250
HbA1C %	r	-0.186
	P	0.035
Insulin (µIU/ml)	r	-0.292
	P	0.001
HOMA-IR	r	-0.230
	P	0.009

FBG= *Fasting blood Glucose*, HbA1C= *Hemoglobin A1c*, *HOMA-IR =homeostatic model assessment-insulin resistance*

Irisin well recognized that physical exercise motivates the transcriptional co-activator PGC-1α in skeletal muscles that due to health benefits such as decrease of obesity and insulin resistance. (Boström*et al.* 2012).

The current study illustrated a negative correlation between circulating levels of Irisin and the hemoglobin A1C (HbA1c) has been detected. Thus, the Irisin serum concentration may reproduce the metabolic grade of subject suffering from metabolic disorders. Furthermore to glycemic or HbA1c,

'Irisinemia' possibly will also become a novel promising concept working to observer metabolic disorders such as Type2 DM or obesity.

The result of this study showed the glycemic controlled by the increase of irisin concentration because the HbA1c percentage was negatively related with circulating Irisin level and reflected the regulated T2DM and high serum Irisin concentration. This observation was in agreement with Choi *et al.*, 2013 and Sanchis *al.*, 2013, which showed a negative linear correlation (r) between hemoglobin A1c and serum levels of Irisin. This result can be of advantage clinically and medicinally in the management and control of glucose homeostasis level in patients with obese T2DM patients.

Correlation Serum Irisin with insulin resistance:

The results of the present study in table 3.6 showed the high significance with a negative linear correlation between insulin resistance and level of irisin (r=-0.230, P 0.009) as showed in figure (3.1) reflected the possible justifications for the recent outcomes that populations with metabolic disorders but without diabetes showed higher circulating irisin levels compared with healthy controls as focus in previous study (Hee Park *et al.* 2013; Li *et al.* 2015; Norheim *et al.* 2014; Crujeiras *et al.* 2014; Qiu *et al.* 2016) The observed negative association between circulating irisin and IR is to be expected to several possible physiological mechanisms. Where elevated irisin levels are linked with decrease levels of insulin resistance.

Whereas FNDC5expression was significantly higher in fat and skeletal muscle in obesity than normal weight positive control. Thus, secretion of irisin may be improved within a fat derived feedback mechanism in obesity patients.

Secretion of irisin into blood improves insulin resistance by elevation uncoupling protein1(UCP1) gene expression, resultant in brown process coloration or changing white fat to brown PGC1α promotes secretion of irisin, contributing to improvement in oxidative metabolism and mitochondrial biosynthesis. Mitochondria play a significant role in insulin.

This study disagreement with the Park *et al.* 2014 and Viitasalo *et al.* 2015 that shown the raised irisin levels are linked with increased levels of insulin resistance because the positive linear correlation between them (irisin and IR).

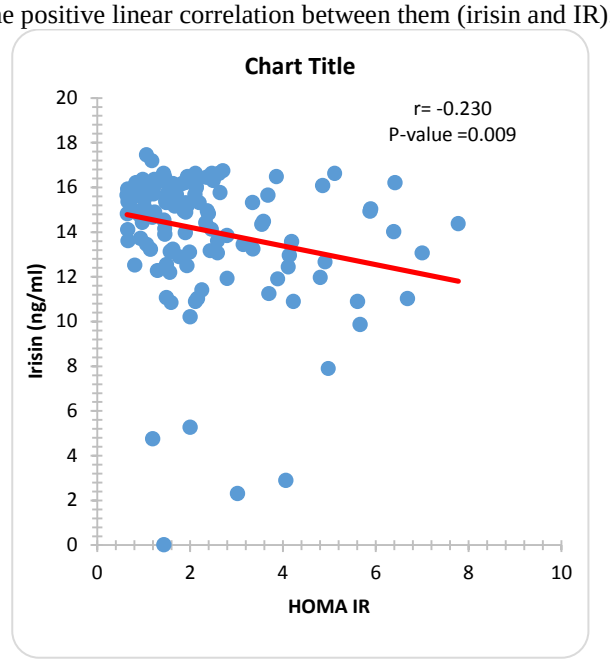

Figure (3.1) correlation between irisin concentrations with HOMA insulin resistance

In another hand, the current study found the decrease of irisin level in the obese patient and increase of glycated HbA1c percentage and insulin resistance value as shown in table 3.2 there was negative correlation and significance difference between the irisin and IR. These results described the risk factor if the irisin levels remained decrease and IR increase and this due to elevated risk of IR with weight gain and that irisin could decrease the insulin resistance beginning, which is associated with weight regain.

The present study agree with, Moreno-Navarrete *et al.* proved a negative correlation between irisin levels and insulin resistance in men with obesity (Moreno *et al.* 2013; Fukushima, *et al.* 2016).

Whereas, this agree with the Crujeiras *et al.* that guessed the energy limit could be risky for several obese subject, because it may encourage IR and elevated the opportunity to T2DM incidence in the future. In this regard, irisin might aid as a potential prognostic indicator and/or a possible therapeutic target in the future and it known that Irisin elevation total energy expenditure.(Crujeiras 2014) In another study was opposed with our result where thepositive correlation observed between circulating irisin and total circulating insulin levels (Stengel, *et al.* 2013).

Insulin resistance may also be interconnected with irisin secretion, for the reason that an increase in irisin promote energy utilization, which contributes to weight loss, fat reduction and enhanced insulin resistance(Bostrom *et al.* 2012;.Fukushima, *et al.* 2016).

Table 3.5 Correlation of irisin with Lipid profile

Correlation parameter		TG (mg/ml)	TC (mg/ml)	HDL-C (mg/ml)	VLDL (mg/ml)	LDL (mg/ml)
Irisin (ng/ml)	R	0.019	-0.007	0.079	0.019	-0.027
	P-value	0.829	0.936	0.375	0.829	0.759

TG= *triglyceride,* TC= *total cholesterol,* VLDL= *very low density lipoprotein,*
LDL= *low density lipoprotein,* HDL-C= *high density lipoprotein-cholesterol, Irisin= novel myokin.*

And some studies suggested that irisin plays an central role in metabolic syndrome or insulin resistance (Yan *et al.* 2014). The regarding of system, PGC1α activated may elevate expression of FNDC5, as a precursor of irisin, helping secretion into blood stream. FNDC5 is noticed in kidney and in skeletal muscle, liver, fat, heart, blood vessels, and lung (Kurdiova *et al.* 2014;Huh *et al.* 2012; Moreno *et al.* 2013; Aydin *et al.* 2014).

3.2.4 Circulation of Serum Irisin with lipid profile in obese patient:

Estimation of levels of irisin in serum by ELISA technique the impact of exercise on serum levels of irisin was subsequently investigated by ELISA with an antibody recognize the 112 amino acids of irisin in many experiments. (Zhang *et al.* 2017).

Correlation of the Serum Irisin in present study showed no observable association with lipid profile parameters, where appear lowest positive relationship with the serum triglyceride (r=0.019, P=0.829), HDL-C (r=0.079, 0.375),Low-density lipoprotein and (r=0.019, P=0.759) respectively that showed no significance with irisin circulation level. In addition, negative and no significant correlation result of total cholesterol (r=-0.007, P=0.936), very low-density lipoprotein (-0.027, P=0.759) for the obese individual as showed in table (3.5)

Other studies reported a similar finding, weakening to demonstrate any correlation between serum Irisin and serum triglycerides, Cholesterol, LDL and VLDL of the obese patient. (Yeon-Kyung *et al.* 2013).

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