Is Irisin a Phenotypic Parameter in Over-Weight Women with Polycystic Ovary Syndrome?

Shaden M.H. Mubarak[1], Hanaa Addai Ali[2]

[1]Post Graduate, College of Pharmacy, University of Kufa, Ira, [2]Proffesor Dr. Department of Chemistry, College of Science, University of Kufa, Iraq

Abstract

Polycystic ovary syndrome (PCOS) is the most public hormonal chaos and the causesthe infertility in the women of reproductive age, offering a varied set of clinical parameters.Irisin had assumed to have a duty in metabolic conditions and PCOS. However, the correlation between irisin and metabolic conditions in PCOS is not clear.The purpose of this control cases study was to evaluate the plasma levels of Irisin in women with overweight PCOS and its correlations with other phenotypes parameters of PCOS. The study involved 90 PCOS women and 40 control healthy women. The PCOS womenwere diagnostic by BMI as overweight. Statistical analysis was performed by using by the SAS (2012) program[1]**.**Chiefresults measure was to determinethe plasma Irisin levels in overweight cases. In addition, some phenotypic and anthropometric parametersincluding BMI, lipid profile, sex hormones, FBG, Insulin, and HOMA-IRhad measured in groups of the study. Results offasting Irisin levels showed significantly elevated differences in overweight PCOS women as compared to the levels in overweight control women(P<0.047).The plasma Irisin levels in overweight PCOS womenshowed significantly positively correlated with BMI,FBG, HOMA-IR, FSH,lipid profile except HDLc and LH/FSH ratioexhibited significantly negatively correlated (P<0.01). Even though there is as until now no proof for a causal association between irisin andPCOS, it is potential that the alterations in Irisin concentrations maybe considered as a phenotype parameter for the diagnosis or development of PCOS, and may act a new PCOS test to follow this syndrome under diverse management of treatments.

Keywords: *Polycystic ovary syndrome, PCOS, irisin, BMI, IR, HOMA-IR, lipid profile, myokines, anovulation, infertility.*

Introduction

Polycystic ovary syndrome (PCOS) is not a disease, It is a syndrome that means a group of phenotypic characteristics that may increase in severity or diminish in appearance, variously linking with lack a fixed reason on which the recognition could be used "gold standard"[2]. PCOS is a complex trouble state includes a set of signs. The most chief of these signs arehyperandrogenemia (HA), Ovulatory Dysfunction (oligo- or anovulation) (OD) and polycystic ovary morphology[3]. However the etiology of PCOS is up to now unknown, but ancollaborationof genetic factors and environmental factors mayplay synergistically as the dominanteffect to its clinical parametersappearance[4].Irisin was announced for the first once in 2012 by the investigation set of Spiegelman from Harvard University, which were exposed and described a small peptide produced in skeletal muscles (SkM) in the company of action-encouraged and is potent to achieve browning fatty [5]. Irisin term derives from the Greek go-between spirits Iris, which encoded byfibronectin type III domain containing 5 (*FNDC5*) gene**.** It is anovel hormone-like glycosylated protein, which is mainly yielded by physical exercise (PhE) of SkM tissues. Though practice has been displayed to rise

Corresponding Author:
Hanaa Addai Ali
Proffesor Dr. Department of Chemistry, College of Science, University of Kufa, Iraq
e-mail: muthanahana74@gmail.com

Irisin level circulation, the stimulate of PhE strength on Irisin production still vague [6,7]. It is expressed in the ovarian tissue, placenta and newborn rope serum. Besides, Irisin is a fresh and hopeful hormone for IR and T2DM [8,9]. In another hand PCOS is the HA, IR state-owned, similar fatness and T2DM [10]. While earlier investigations have recommended an association the Irisin and the metabolic factors related with fatness and T2DM, the outcomes have been varying[11]. Several studies proved this Irisin ranks were meaningfully upper in PCOS than normal females and linked with HA advised that Irisin can be a key analyst of HA, metabolic syndrome (MetS) and IR[12,13]. Despite the fact that some additional investigations stated parallel[14,15] or lesser [16] blood Irisin ranks in PCOS than non-PCOS females.

Study Design and Subjects: The current dissertation is a case-control study related to females with PCOS as cases and controls with regular reproductive past. The Rotterdam criteria-2003[3] was assumed to ninety PCOS females (n=90)withages reached between (19-42) years with a Mean±SE (29.16 ± 0.53) years.PCOS and control groups were identified by a gynaecologists of the "Fertility Center in AL-Sadder Teaching Hospital in Najaf Governorate", and "Infertility center in Maternity and Children Hospital in Babylon Governorate", Iraq during the duration from July 2017 to August 2018. The identification was complete agreeing the criteria of identification of PCOS. Doubted PCOS causes were omitted. Controller group has forty (n=40) womenwhich ages reached between (19-42 years) with a Mean±SE(27.40 ± 0.88) were nominated deprived of any past of OD,sterility, and clinical marks of HA.They have regular menstruation period, with normal ovaries as they were observed by the gynaecologists which no take contraceptive, not smokers with no past of somewhat disease.

Intended for the controller set they were the age,weight and length. Females agonized from diseases DM,autoimmune diseases, thyroid maladies, high blood pressure, CVD, prolonged kidney diseases and had historical of using someadditional therapy for example Hypolipidemic agents, medications that prevent pregnancy or ovulation inducement, cortisone-like medicines (corticosteroids), lowering the glucose level and treating hypertension medications within6 months were omitted. All causes of PCOS and healthy females were married. The measurements in these studies included anthropometry [length, waist to hip ratio (WHR), and BMI]. All of the investigated sets were verified within 2nd to 3rd days of menstruation.The lab experiments were passed out in laboratories of the College of Pharmacy at the University of Kufa.

Blood Samples Collection: Venous blood samples were gathered from females' donors to the study (n=130, PCOS and controls). Plasma samples were got after centrifugation EDTA tubes as stated by standard protocols,thenstored at −20 °C until examination [17].

Phenotypes Analysis: Irisin, FSH, LH, E2, PRL, and Insulin concentrations were quantified fixed in employing trade enzyme-linked immunosorbent (ELISA) assays (Elabscience, USA), and (abcam, U.S.A) for Total Testosterone levels, in conformity with the maker's instructions.The concentrations of fasting; TG, cholesterol, LDLc, VLDLc, HDLc, and FBG were measured by traditional spectrophotometry procedures(Biolabo, France),in conformity with the maker's instructions.Besides anthropometric measures; WHR and BMI[18]. The homeostatic model assessment (HOMA-IR)[19], lipids ratios, and LH/FSH ratio were calculated.

Statistical Analysis: The statics that works in the current study are (mean ±SD, the T-test for two variables and ANOVA test by the SAS (2012) program[1]. The ranking of significance, which applied, was ≤ 0.05 in all-statistical analysis. Estimate of correlation coefficient between variables in this study.

Results

The phenotypes results of Irisin levels in PCOS group compared to the control showed high levels with significant differences (P<0.047). In addition, all of the following phenotypes: FBG, Insulin, HOMA-IR, lipids profile, lipids ratios, sex hormones, LH/FSH ratio and BMI showed highly significant differences at least (*P*<0.001) between the study categories**(Table I)**. The correlation study carried out between irisin and the rest phenotypes results. Irisin correlation showed positivelysignificant correlation with BMI, lipid profile, FSH, FBG, HOMA-IR. While Irisin showed negatively significant correlation with LH/FSH ratioand HDLc. However the rest of thephenotypes gave a variety andpredictable of correlation relationships**(Table II) (Table III)(Table IV).**

Table I. The Comparison Between phenotypes features of Control and PCOS Patients' Groups

Parameters	Mean ± SE		P-Value
	Control	Patients	
Number	40	90	-
Irisin (ng/ml)	9.11 ± 0.39	9.67 ± 0.22	0.047*
Age (year)	27.40 ± 0.88	29.16 ± 0.53	**0.078** NS
WHR	0.810 ± 0.011	0.827 ± 0.006	**0.134** NS
BMI (kg/m2)	25.00 ± 0.31	29.80 ± 0.42	**0.0001****
FSH (mlU/ml)	6.70 ± 0.30	5.39 ± 0.17	0.0001***
LH (mlU/ml)	4.75 ± 0.29	9.71 ± 0.23	0.0001***
LH/FSH ratio	0.760 ± 0.06	2.093 ± 0.11	0.0001***
E2 (pg/ml)	32.52 ± 1.64	25.37 ± 1.25	0.001***
Prolactin (ng/ml)	12.25 ± 0.46	31.24 ± 0.89	0.0001***
Total Testosterone (nmol/L)	1.005 ± 0.07	2.971 ± 0.10	0.0001***
FBG (mg/dl)	91.17 ± 1.19	117.03 ± 2.01	0.0001***
Insulin (ng/ml)	6.96 ± 0.07	20.7 ± 0.6	0.0001***
HOMA-IR	0.261 ± 0.01	1.74 ± 0.06	0.0001***
Triglyceride(mg/dl)	119.47 ± 5.53	159.96 ± 3.11	0.0001***
Total Cholesterol(mg/dl)	170.55 ± 2.90	187.16 ± 3.58	0.0043**
HDLc(mg/dl)	61.55 ± 1.67	50.40 ± 0.76	0.0001***
VLDLc(mg/dl)	23.90 ± 1.12	32.01 ± 0.61	0.0001***
LDLc(mg/dl)	85.02 ± 3.59	104.78 ± 3.79	0.0017**
Cholesterol/HDLc Ratio	2.86 ± 0.10	3.84 ± 0.12	0.0001***
LDLc/HDLc Ratio	1.462 ± 0.09	2.182 ± 0.11	0.0001***
VLDLc/HDLc Ratio	0.405 ± 0.02	0.656 ± 0.02	0.0001***

SE: Standard Error, *P*-Value: Probability, **: (*P*<0.01), ***: High Significant (*P*<0.001), NS: Non-Significant, Numbers: numbers of group, WHR: Waist/Hip Ratio, BMI: Body Mass Index, FSH: Follicular Stimulating Hormone, LH: Luteinizing Hormone, E2:Estradiol, FBG: Fasting Blood Glucose, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance,HDLc: High Density Lipoprotein Binding Cholesterol, VLDLc: Very Low Density Lipoproteins Binding Cholesterol, LDLc: Low Density Lipoprotein Binding Cholesterol.

Table II. The Correlation of Irisin, Sex Hormones, and lipid profile Levels with Anthropometric and Glycemic Parameters in PCOS Patients

Parameters	Correlation Coefficients–r					
	BMI	FBG	HOMA-IR	Insulin	WHR	Age
Irisin	0.40**	0.29 **	0.17 *	0.04 NS	0.09 NS	0.14 NS
FSH	0.30 **	-0.05 NS	-0.12 NS	-0.18 *	0.04 NS	0.27 **
LH	0.06 NS	0.24 **	0.39 **	0.43 **	-0.02 NS	0.03 NS
LH/FSH ratio	-0.17 NS	0.12 NS	0.25 **	0.31 **	-0.05 NS	-0.11 NS
E2	-0.01 NS	-0.02 NS	-0.19 *	-0.27 **	0.14 NS	-0.12 NS
Prolactin	0.41**	0.46 **	0.51 **	0.46 **	0.09 NS	0.04 NS
Total Testosterone	0.49 **	0.48 **	0.56 **	0.50 **	0.14 NS	0.08 NS
Triglyceride	0.74**	0.49 **	0.48 **	0.35 **	0.26 **	0.13 NS
Total cholesterol	0.66**	0.38 **	0.28 **	0.14 NS	0.28 **	0.07 NS
HDLc	-0.50**	-0.42 **	0.39 **	-0.31 **	-0.18 *	-0.23 **
VLDLc	0.74**	0.48 **	0.34 **	0.35 **	0.26 **	0.13 NS
LDLc	0.59**	0.36 **	0.51 **	0.14 NS	0.25 **	0.11 NS
Cholesterol/HDLc Ratio	0.68**	0.45 **	0.39**	0.23 **	0.24 **	0.16 *

*: (*P*<0.05), **: (*P*<0.01), NS: Non-Significant,WHR: Waist/Hip Ratio, BMI: Body Mass Index, FSH: Follicular Stimulating Hormone, LH: Luteinizing Hormone, E2:Estradiol, FBG: Fasting Blood Glucose, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance, HDLc: High Density Lipoprotein Binding Cholesterol, VLDLc: Very Low Density Lipoproteins Binding Cholesterol, LDLc: Low Density Lipoprotein Binding Cholesterol.

Table III. Correlation of Irisin and Hormones Levels with Lipid Profile Levels in PCOS Patients

Parameters	Correlation coefficients –r						
	FSH	LH	LH/FSH	E2	Prol	Total Testo	Irisin
Triglyceride	0.13 NS	0.15 NS	-0.02 NS	-0.13 NS	0.38 **	0.47 **	0.43 **
Total chol	0.23 **	0.04 NS	-0.08 NS	0.07 NS	0.25 **	0.27 **	0.25 **
HDLc	-0.04 NS	-0.29 **	-0.12 NS	0.16 *	-0.41 **	-0.39 **	-0.24 **
VLDLc	0.12 NS	0.15 NS	-0.01 NS	-0.13 NS	0.39 **	0.47 **	0.43 **
LDLc	0.19 *	0.09 NS	-0.03 NS	0.05 NS	0.27 **	0.26 **	0.21 **
Chol/HDLc Ratio	0.17 *	0.15 NS	-0.02 NS	-0.02 NS	0.35 **	0.38 **	0.32 **

SE: Standard Error, P-Value: Probability, * (P<0.05), ** (P<0.01),NS: Non-Significant **: (P<0.01), NS: Non-Significant, FSH: Follicular Stimulating Hormone, LH: Luteinizing Hormone, E2:Estradiol, Prol: Prolactin, Total Testo: Total testosterone, Chol: Cholesterol, HDLc: High Density Lipoprotein Binding Cholesterol, VLDLc: Very Low Density Lipoproteins Binding Cholesterol, LDLc: Low Density Lipoprotein Binding Cholesterol**.**

Table IV. Correlation Irisin with Other Hormones Levels in PCOS Patients

Hormones	Correlation -r with Irisin	Level of sig.
FSH	0.26	**
LH/FSH Ratio	-0.29 **	**
LH	-0.15	NS
E2	-0.05	NS
Prolactin	0.14	NS
Total Testosterone	0.13	NS

P-Value: Probability **: (*P*<0.01), NS: Non-Significant, FSH: Follicular Stimulating Hormone, LH: Luteinizing Hormone, E2:Estradiol.

Discussion

This study showed that PCOS women have high irisin concentrations in overweight PCOS women when compared to corresponding controls even after adjusting for confusingissues as age, and WHR. These changes are parallel with the main presentation of HA lead to appearance PCOS, and are related to elevated levels of LH, LH/FSH ratio and lipid profile. Therefore, irregular of irisin levels could illustrate novel PCOS phenotypes. Additionally, our information recommended that these changes might participate in the progress of comorbidities, such as IR, dyslipidemia, and obesity in PCOS women. In spite of the pathway by it the irisin levels are high in PCOS women continue investigated, this information shows that the metabolizing forms of PCOS women are different in nature from those of T2D or obesity patients even though PCOS women have a trend advanced T2D in future[20,21]. The determination of high irisin levels in PCOS women is harmonic with modern information revealed high irisin levels in cases with MetS[22]. In view of the fact that irisin remarkably elevates energy expenditure in brown and beige adipose tissues, it is feasible that irisin raised in PCOS women as a defensive system act against surplus energy influx[23]. Otherwise, the raised irisin level can act as an "irisin resistance" condition[24,25], similar that of IR in that elevated Insulin levels failed to influence the required result.

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