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Serum betatrophin and irisin levels in patients with polycystic ovary syndrome with and without insulin resistance

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a heterogeneous disorder with significant metabolic components, particularly insulin resistance (IR). Irisin and betatrophin have been proposed as novel metabolic regulators.

Methods: Patient selection was performed retrospectively, while the study was designed prospectively. Sixty women (20 PCOS, 20 PCOS+IR, 20 controls) were included. Plasma irisin and betatrophin levels were measured using ELISA. Clinical, biochemical, and hormonal parameters were analyzed, and correlations with metabolic markers were evaluated.

Results: Irisin levels were significantly higher in the PCOS+IR group, while betatrophin levels were significantly lower in both PCOS groups compared to controls. Irisin showed a positive correlation with body mass index (BMI), whereas betatrophin showed no significant correlation with BMI. No correlation was observed between irisin and betatrophin.

Conclusion: Irisin and betatrophin exhibit distinct and independent alterations in PCOS. These biomarkers may contribute to improved metabolic phenotyping and risk assessment in PCOS.

Keywords: polycystic ovary syndrome, irisin, betatrophin

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age and is characterized by a broad clinical spectrum, including hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology [1]. However, PCOS is not limited to a reproductive disorder but represents a complex condition with a prominent metabolic component. In particular, insulin resistance (IR) and the accompanying hyperinsulinemia play a central role in the pathophysiology of PCOS, they contribute to hyperandrogenism by affecting ovarian function and increase the risk of dyslipidemia, obesity, and type 2 diabetes, thereby influencing long-term cardiometabolic outcomes [2, 3]. Therefore, metabolic phenotyping in PCOS is of critical importance for clinical risk stratification [4].

In recent years, various adipokines and myokines associated with energy homeostasis, glucose metabolism, and inflammation have been proposed as potential mediators in the pathogenesis of PCOS [5]. These molecules may contribute to the development of IR by modulating insulin signaling in peripheral tissues and may also be detected at increased levels as part of a compensatory response under conditions of metabolic stress. In this context, irisin, also referred to as an "adipomyokine," is a peptide secreted from multiple tissues, primarily skeletal muscle and adipose tissue, and has been associated with energy expenditure, adipose tissue function, and glucose metabolism [6]. Recent reviews emphasize that irisin may represent an adaptive response that increases particularly in the presence of IR and metabolic stress [7, 8]. However, findings regarding the relationship between irisin levels and IR, obesity, and metabolic syndrome remain heterogeneous, with variable results reported across different populations [9, 10].

Betatrophin was initially associated with glucose metabolism and pancreatic β-cell function; however, subsequent studies have suggested a closer relationship with lipid metabolism, hepatic energy balance, and insulin sensitivity [11, 12]. Recent reviews indicate that the role of betatrophin in β-cell proliferation is limited and that it should primarily be considered a molecule involved in metabolic regulation and IR [13]. Studies investigating betatrophin levels in PCOS are limited, and existing data have reported inconsistent results, particularly according to the presence of IR [14]. Similarly, although several studies have evaluated the relationship between irisin levels and IR in PCOS, studies assessing irisin and betatrophin together remain relatively scarce.

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In this study, plasma irisin and betatrophin levels were evaluated in patients with PCOS with and without IR, and the findings were compared with those of a healthy control group. The aim of this study was to investigate the potential impact of IR on irisin and betatrophin levels in PCOS and to assess the potential role of these molecules in the metabolic phenotyping of PCOS.

MATERIALS AND METHODS

This study was conducted at the Obstetrics and Gynecology Outpatient Clinic at Turgut Özal University Hospital between December 2014 and October 2015. The study protocol was approved by the Ethics Committee at Turgut Özal University and was carried out in accordance with the ethical principles of the Declaration of Helsinki. All participants were informed about the study, and written informed consent was obtained. Patient selection was performed retrospectively, while the study was designed prospectively.

A total of 65 patients who presented to our clinic with a preliminary diagnosis of PCOS were initially enrolled in the study. Among these, 61 patients who fulfilled the Rotterdam criteria for PCOS were identified and included in the final analysis.

Based on the results of laboratory evaluations, these patients were further stratified into two groups: PCOS patients with IR and PCOS patients without IR. Patient recruitment was terminated once each subgroup reached a sample size of 20 individuals.

In addition, 20 healthy volunteers with demographic characteristics comparable to the PCOS group were selected from individuals presenting to the outpatient clinic and were included as the control group.

PCOS was diagnosed based on the presence of at least two of the following criteria according to the Rotterdam consensus [1]; oligo-amenorrhea (menstrual intervals ≥ 35 days or ≤ 8 menstrual cycles per year), clinical or biochemical hyperandrogenism (acne, hirsutism, androgenic alopecia, acanthosis nigricans, or elevated plasma testosterone levels), and polycystic ovarian morphology on ultrasonography (≥ 12 follicles measuring 2-9 mm in diameter and/or ovarian volume > 10 mL in at least one ovary).

Inclusion criteria for the healthy control group were as follows: age between 18 and 40 years, regular menstrual cycles, absence of clinical or biochemical signs of hyperandrogenism, normal ovarian morphology on ultrasonography, and no history of systemic disease or regular medication use.

Exclusion criteria included endocrine disorders that could cause amenorrhea or hirsutism (such as late-onset congenital adrenal hyperplasia, cushing syndrome, prolactinoma, and hypothyroidism), use of medications affecting IR, hereditary or acquired muscle diseases, chronic systemic conditions such as diabetes mellitus and hypertension, history of malignancy, alcohol or smoking, history of pancreatitis, and use of hormonal therapies–except for the use of oral contraceptives for menstrual regulation–ovulation induction agents, glucocorticoids, antiandrogens, or antihypertensive drugs within the last 6 months.

Body weight of all participants was measured after a 12-hour overnight fast using a standard scale, with participants wearing light clothing and no shoes. Height was measured using a stadiometer, and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

The degree of hirsutism was assessed using the Ferriman – Gallwey scoring system. Nine anatomical areas were scored from 0 to 4, and a total score ≥ 8 was considered indicative of hirsutism [15].

Blood samples were obtained from all participants during the early follicular phase of a spontaneous or induced menstrual cycle (days 3-5), following at least 8 hours of fasting, between 08:00 and 10:00 a.m. Fasting plasma glucose, fasting insulin levels, lipid profile, complete blood count, urea, creatinine, and hormonal parameters (FSH, luteinizing hormone [LH], estradiol, prolactin, TSH, total testosterone, DHEA-SO_4, and 17-hydroxyprogesterone) were analyzed on the same day. Hormonal and insulin measurements were performed using an electrochemiluminescence immunoassay method (Roche Diagnostics GmbH, Mannheim, Germany), while biochemical parameters were analyzed using an automated analyzer (Roche-Hitachi 717-902, Mannheim, Germany).

IR was calculated using the HOMA-IR formula [fasting glucose (mg/dL) × fasting insulin (µU/mL)/405] [16]. A HOMA-IR value ≥ 2.48 was accepted as indicative of IR [17]. All participants underwent a 75-g oral glucose tolerance test (OGTT), and plasma glucose levels were measured at 0 and 120 minutes. Results were evaluated according to the ADA 2003 criteria [18]. IR was defined as a HOMA-IR value ≥ 2.48 and/or a 120-minute OGTT plasma glucose level ≥ 140 mg/dL.

For the analysis of plasma betatrophin and irisin levels, venous blood samples were obtained from all participants during the early follicular phase (days 3-5) of a spontaneous or induced menstrual cycle, following approximately 8 hours of fasting, between 08:00 and 10:00 a.m. Blood samples were collected into potassium EDTA tubes containing a protease inhibitor (aprotinin). The samples were centrifuged at 1,500-2,000 rpm for 10 minutes, and plasma was separated. Plasma samples were stored at -80°C until analysis. Plasma betatrophin and irisin levels were measured simultaneously using a microplate enzyme-linked immunosorbent assay (ELISA) (DRG Diagnostics, USA). Plasma irisin and betatrophin levels were expressed in ng/mL.

Statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). The distribution of variables was assessed using the Shapiro-Wilk test and was found to be non-normal. Continuous variables were expressed as median (interquartile range), and categorical variables as number and percentage. The Kruskal–Wallis test was used for comparisons among groups, and for variables with significant differences, the Mann-Whitney U test with Bonferroni correction was applied for pairwise comparisons. Categorical variables were analyzed using the chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 60 women were included in the study, comprising 20 patients with PCOS, 20 patients with PCOS and IR (PCOS+IR), and 20 healthy controls. There were no significant differences among the groups in terms of age, gravida, parity, or abortion history (**Table 1**). However, height was significantly lower in

Table 1. Clinical and demographic data of the participants

Parameter	Control (n = 20)	PCOS (n = 20)	PCOS+IR (n = 20)	p
Age (year)	24.0 (16)	27.5 (13)	25.5 (16)	0.645
Gravida	0.0 (3)	0.0 (2)	0.0 (2)	0.098
Parity	0.0 (2)	0.0 (1)	0.0 (1)	0.347
Abortions	0.0 (1)	0.0 (1)	0.0 (2)	0.092
Height (cm)	168.0 (18)	162.5 (23.1)	161.0 (34.2)	**0.006[1]**
Weight (kg)	60.5 (31)	61.0 (36)	68.5 (119)	**0.004[1]**
BMI (kg/m^2)	21.2 (8.6)	23.1 (10.9)	26.0 (29.1)	**< 0.001[2]**

Note. Data are given as median (interquartile range); $p < 0.05$ accepted as statistically significant; [1]Significant difference between the control and PCOS+IR groups; & [2]Significant difference between the control and PCOS groups, and between the control and PCOS+IR groups

Table 2. Biochemical and hormonal parameters of the participants

Parameter	Control (n = 20)	PCOS (n = 20)	PCOS+IR (n = 20)	p
Fasting blood glucose (mg/dL)	87.5 (25)	88.5 (23.1)	88.0 (112)	0.578
Hemoglobin (g/dL)	13.0 (3.9)	12.9 (3.1)	13.1 (4)	0.744
WBC (×10^3/μL)	6.5 (7)	6.4 (6.8)	7.5 (7)	**0.029[2]**
Platelet (×10^3/μL)	281.0 (185)	246.5 (157)	285.5 (246)	0.083
Total cholesterol (mg/dL)	170.5 (76)	154.0 (113)	187.5 (171)	0.172
Triglyceride (mg/dL)	66.0 (59)	65.0 (81)	96.0 (324)	**0.017[2]**
LDL (mg/dL)	98.0 (72)	82.5 (109)	110.0 (90)	0.174
VLDL (mg/dL)	13.0 (12)	13.0 (17)	19.5 (65)	**0.015[2]**
HDL (mg/dL)	57.5 (64)	58.5 (39)	50.5 (68)	0.188
FSH (mIU/mL)	6.5 (5.6)	5.9 (6.8)	5.6 (4.1)	0.222
LH (mIU/mL)	5.6 (7.4)	8.2 (55.2)	5.9 (9.8)	**0.003[1]**
E2 (pg/mL)	36.0 (76.7)	41.0 (453)	33.5 (42)	0.150
TSH (μIU/mL)	2.6 (3.8)	1.8 (4.8)	1.8 (4.2)	0.453
Prolactin (ng/mL)	17.8 (53.3)	14.3 (41.9)	12.7 (36.5)	0.296
Insulin (μIU/mL)	8.8 (6.2)	6.8 (6.5)	15.5 (111)	**< 0.001[2, 3]**
HOMA-IR	1.9 (1.3)	1.2 (1.4)	3.2 (11.7)	**< 0.001[2, 3]**
OGTT 0 min (mg/dL)	88.0 (25)	88.0 (23)	88.0 (117)	0.819
OGTT 2h (mg/dL)	87.0 (53)	85.0 (61)	108.5 (128)	**0.001[2, 3]**
Total testosterone (ng/dL)	13.9 (44.3)	37.1 (175.3)	35.7 (52.7)	**< 0.001[1, 2]**
Progesterone (ng/dL)	1.0 (1.3)	1.1 (1.1)	1.0 (1.5)	0.500
DHEAS (μg/dL)	233.0 (308)	288.0 (357)	285.4 (529)	0.061
Urea (mg/dL)	20.5 (23)	23.0 (24)	21.0 (21)	0.435
Creatinine (mg/dL)	0.7 (0.3)	0.7 (0.5)	0.6 (0.3)	0.788

Note. LDL: Low-density lipoprotein; VLDL: Very low-density lipoprotein; HDL: High-density lipoprotein; FSH: Follicle-stimulating hormone; E2: Estradiol; TSH: Thyroid-stimulating hormone; HOMA-IR: Homeostasis model assessment of insulin resistance; DHEAS: Dehydroepiandrosterone sulfate; Data are given as median (interquartile range); $p < 0.05$ accepted as statistically significant; [1]Significant difference between the control and PCOS groups; [2]Significant difference between the control and PCOS+IR groups; & [3]Significant difference between the PCOS and PCOS+IR groups

both the PCOS and PCOS+IR groups compared to controls (p = 0.006).

In addition, weight and BMI were significantly higher in the PCOS+IR group compared to the control group (p = 0.004 and p < 0.001, respectively). In the clinical evaluation, oligomenorrhea, acne, hirsutism, and polycystic ovarian morphology on ultrasonography were observed significantly more frequently in the PCOS and PCOS+IR groups compared to the control group (p < 0.05 for all).

Table 3. Distribution of betatrophin and irisin levels by groups

Parameter	Control (n = 20)	PCOS (n = 20)	PCOS+IR (n = 20)	p
Betatrophin (ng/mL)	24.9 (70.2)	4.6 (61.1)	3.7 (48.3)	**0.008[1, 2]**
Irisin (ng/mL)	158.1 (207.7)	176.1 (230.1)	211.8 (253.4)	**0.022[2]**

Note. Data are given as median (interquartile range); $p < 0.05$ accepted as statistically significant; [1]Significant difference between the control and PCOS groups; & [2]Significant difference between the control and PCOS+IR groups

Table 4. Differential correlation of irisin and betatrophin with metabolic parameters in PCOS

Parameter	Irisin (ρ)	p	Betatrophin (ρ)	p
BMI (kg/m^2)	0.309	**0.016**	0.033	0.801
Insulin (μIU/mL)	0.121	0.358	-0.186	0.156
HOMA-IR	0.171	0.191	-0.251	0.053
Triglyceride (mg/dL)	0.267	**0.039**	0.090	0.494
VLDL (mg/dL)	0.282	**0.029**	0.062	0.637
HDL (mg/dL)	-0.310	**0.016**	0.091	0.487
Irisin ↔ betatrophin	-	-	-0.028	0.831

Note. HOMA-IR: Homeostasis model assessment of insulin resistance; VLDL: Very low-density lipoprotein; HDL: High-density lipoprotein; ρ: Spearman correlation coefficient; Data are given as median (interquartile range); & $p < 0.05$ accepted as statistically significant

Plasma biochemical and hormonal parameters were compared among the control, PCOS, and PCOS+IR groups (**Table 2**). White blood cell (WBC) count was significantly higher in the PCOS+IR group compared to controls (p = 0.029). Triglyceride levels were also significantly elevated in the PCOS+IR group compared to the control group (p = 0.017), accompanied by higher VLDL levels (p = 0.015). LH levels were significantly higher in the PCOS group compared to controls (p = 0.003). Fasting insulin levels were markedly increased in the PCOS+IR group compared to both the control and PCOS groups (p < 0.001), and HOMA-IR values were significantly higher in the PCOS+IR group compared to both groups (p < 0.001). In addition, 2-hour glucose levels during the oral glucose tolerance test (OGTT 2h) were significantly elevated in the PCOS+IR group compared to both control and PCOS groups (p=0.001). Total testosterone levels were significantly higher in both PCOS and PCOS+IR groups compared to the control group (p < 0.001). No statistically significant differences were observed among the groups for other biochemical and hormonal parameters.

Plasma betatrophin and irisin levels were compared among the control, PCOS, and PCOS+IR groups (**Table 3**). Betatrophin levels were significantly lower in both the PCOS and PCOS+IR groups compared to the control group (p = 0.008). In contrast, irisin levels were significantly higher in the PCOS and PCOS+IR groups compared to controls (p = 0.022).

Irisin levels showed a positive correlation with BMI, triglyceride, and VLDL levels, and a negative correlation with HDL (p < 0.05 for all) (**Table 4**). No significant association was found between irisin and insulin or HOMA-IR. Betatrophin levels were not significantly correlated with metabolic parameters. Additionally, no correlation was observed between irisin and betatrophin levels.

DISCUSSION

In this study, we evaluated changes in irisin and betatrophin levels in women with PCOS according to the presence of IR. Our findings demonstrated that irisin levels were significantly higher in the PCOS+IR group, whereas betatrophin levels were significantly lower in both the PCOS and PCOS+IR groups compared to the control group. While irisin levels showed a positive correlation with BMI, no significant correlation was observed between betatrophin levels and BMI.

Irisin is an exercise-induced myokine derived from FNDC5 that plays a key role in energy metabolism by promoting the browning of white adipose tissue and increasing energy expenditure. It contributes to glucose homeostasis by enhancing glycogen synthesis and suppressing hepatic gluconeogenesis, thereby improving insulin sensitivity [19]. Significant elevation of irisin levels in the PCOS+IR group, along with its positive correlation with BMI, suggests that irisin may increase as a compensatory response under conditions of increased metabolic load associated with adiposity and may reflect a potential "irisin resistance" phenomenon.

Betatrophin is a liver- and adipose-derived hormone involved in energy metabolism, particularly regulating lipid metabolism through inhibition of lipoprotein lipase activity and modulation of triglyceride levels. It has been closely associated with IR and is thought to be overregulated in metabolic conditions such as obesity and type 2 diabetes, potentially serving as a compensatory response to metabolic stress [20]. In our study, the consistently lower betatrophin levels in all PCOS patients and the lack of correlation with BMI support the notion that reduced betatrophin levels may be independent of obesity and instead related to PCOS-specific hormonal and metabolic alterations or an impaired response within the hepato-adipose axis under chronic metabolic stress.

Previous studies investigating the relationship between irisin and PCOS have generally reported increased irisin levels in patients with PCOS. It was observed higher serum irisin, total cholesterol, LDL, and visceral fat levels in 33 patients with PCOS compared to 32 healthy controls [21]. Similarly, it was reported significantly elevated irisin levels in 56 patients with PCOS compared to 32 healthy individuals [22]. It was found that, in a study comparing 45 obese PCOS patients, 45 normal-weight PCOS patients, and 30 healthy controls, increased irisin levels in all PCOS groups [23]. Consistent with the literature, our study also demonstrated elevated irisin levels in PCOS patients with IR.

Studies investigating the relationship between betatrophin and PCOS have reported variable and sometimes conflicting results. While some studies have demonstrated increased betatrophin levels in patients with PCOS compared to healthy controls [24-26], others have reported decreased levels [27, 28]. It was found lower betatrophin levels in 51 patients with well-established PCOS compared to 47 healthy participants and interpreted this finding as a reflection of impaired hepatic and adipose regulation under chronic metabolic stress in a more advanced PCOS phenotype [27].

These inconsistent findings become more understandable when considering the biological heterogeneity of PCOS. Recent data-driven classification studies have shown that PCOS can be divided into distinct subtypes, including hyperandrogenic, obesity-related, high SHBG, and LH–AMH axis–dominant phenotypes, each associated with significantly different metabolic risk profiles [4]. The majority of existing studies (including ours) rely on the classical Rotterdam criteria for PCOS diagnosis, which likely results in heterogeneous study populations comprising different subtype combinations and may contribute to the variability in reported betatrophin levels. Therefore, future studies incorporating subtype-based analyses are essential to better elucidate the role of betatrophin in the pathophysiology of PCOS.

Our findings suggest that irisin and betatrophin may serve as potential biomarkers for metabolic stratification in patients with PCOS. In particular, irisin may reflect adiposity-related metabolic burden, whereas betatrophin may indicate obesity-independent metabolic dysregulation. Accordingly, the combined evaluation of these markers could provide additional information beyond conventional parameters in identifying high-risk PCOS phenotypes.

Another important finding of our study is that, although irisin and betatrophin levels were significantly altered in the presence of PCOS and IR, no significant correlation was observed between these two markers. This suggests that, rather than representing components of a single shared pathway, irisin and betatrophin may reflect distinct and independent metabolic responses originating from different tissues and regulated by different physiological stimuli.

This study has several limitations. First, the relatively small sample size and the cross-sectional design limit the ability to draw causal inferences from the findings. Second, irisin and betatrophin levels were measured at a single time point, precluding the evaluation of their dynamic changes over time. Finally, potential methodological variability associated with ELISA assays, including inter-kit differences, should be acknowledged, as these may impact the absolute quantification of the measured biomarkers.

Despite these limitations, our study is one of the few to evaluate the differential and independent effects of IR on irisin and betatrophin levels within the same PCOS population. Future studies with larger sample sizes, subtype-based PCOS classification, and longitudinal follow-up are needed to further clarify the roles of these molecules in predicting metabolic risk in PCOS.

CONCLUSION

In conclusion, our findings suggest that irisin and betatrophin exhibit distinct and independent alterations in PCOS, particularly in relation to IR. Elevated irisin levels may reflect a compensatory response to increased metabolic burden, whereas reduced betatrophin levels may indicate impaired hepato-adipose regulation under chronic metabolic stress. These results highlight the potential of these biomarkers in the metabolic characterization of PCOS and warrant further investigation in larger, longitudinal studies.

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Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Christ JP, Cedars MI. Current guidelines for diagnosing PCOS. Diagnostics (Basel). 2023;13(6):1113. https://doi.org/10.3390/diagnostics13061113 PMid:36980421 PMCid: PMC10047373
2. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: An update on mechanisms and implications. Endocr Rev. 2012;33(6):981-1030. https://doi.org/10.1210/er.2011-1034 PMid:23065822 PMCid:PMC5393155
3. Diamanti-Kandarakis E. Insulin resistance in PCOS. Endocrine. 2006;30(1):13-7. https://doi.org/10.1385/ENDO:30:1:13 PMid:17185787
4. Gao X, Zhao S, Du Y, et al. Data-driven subtypes of polycystic ovary syndrome and their association with clinical outcomes. Nat Med. 2025;31(12):4214-24. https://doi.org/10.1038/s41591-025-03984-1 PMid: 41162652 PMCid:PMC12705455
5. Spritzer PM, Lecke SB, Satler F, Morsch DM. Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic ovary syndrome. Reproduction. 2015;149(5):R219-27. https://doi.org/10.1530/REP-14-0435 PMid:25628442
6. Boström P, Wu J, Jedrychowski MP, et al. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012; 481(7382):463-8. https://doi.org/10.1038/nature10777 PMid:22237023 PMCid:PMC3522098
7. Leustean L, Preda C, Teodoriu L, Mihalache L, Arhire L, Ungureanu M-C. Role of irisin in endocrine and metabolic disorders—possible new therapeutic agent? Appl Sci. 2021;11(12):5579. https://doi.org/10.3390/app11125579
8. Martinez Munoz IY, Camarillo Romero EDS, Garduno Garcia JJ. Irisin a novel metabolic biomarker: Present knowledge and future directions. Int J Endocrinol. 2018;2018:7816806. https://doi.org/10.1155/2018/7816806 PMid:30402097 PMCid:PMC6198573
9. Chen JQ, Huang YY, Gusdon AM, Qu S. Irisin: A new molecular marker and target in metabolic disorder. Lipids Health Dis. 2015;14:2. https://doi.org/10.1186/1476-511X-14-2 PMid:25588692 PMCid:PMC4417264
10. Polyzos SA, Anastasilakis AD, Efstathiadou ZA, et al. Irisin in metabolic diseases. Endocrine. 2018;59(2):260-74. https://doi.org/10.1007/s12020-017-1476-1 PMid:29170905
11. Levitsky LL, Ardestani G, Rhoads DB. Role of growth factors in control of pancreatic beta cell mass: Focus on betatrophin. Curr Opin Pediatr. 2014;26(4):475-9. https://doi.org/10.1097/MOP.0000000000000110 PMid: 24905104
12. Luo M, Peng D. ANGPTL8: An important regulator in metabolic disorders. Front Endocrinol (Lausanne). 2018;9:169. https://doi.org/10.3389/fendo.2018.00169 PMid:29719529 PMCid:PMC5913278
13. Abu-Farha M, Abubaker J, Tuomilehto J. ANGPTL8 (betatrophin) role in diabetes and metabolic diseases. Diabetes Metab Res Rev. 2017;33(8). https://doi.org/10.1002/dmrr.2919 PMid:28722798
14. Li S, Liu D, Li L, et al. Circulating betatrophin in patients with type 2 diabetes: A meta-analysis. J Diabetes Res. 2016;2016:6194750. https://doi.org/10.1155/2016/6194750 PMid:26697500 PMCid:PMC4678092
15. Ferrimand D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab. 1961;21:1440-7. https://doi.org/10.1210/jcem-21-11-1440 PMid:13892577 PMCid:PMC12499726
16. Wang Y, Fedorcsák P, Dale PO, Storeng R, Abyholm T, Tanbo T. Simplification of continuous infusion of glucose with model assessment in the evaluation of insulin resistance in women with PCOS. Gynecol Endocrinol. 2001;15(3):192-7. https://doi.org/10.1080/gye.15.3.192.197 PMid:11447730
17. Esteghamati A, Ashraf H, Esteghamati AR, et al. Optimal threshold of homeostasis model assessment for insulin resistance in an Iranian population: The implication of metabolic syndrome to detect insulin resistance. Diabetes Res Clin Pract. 2009;84(3):279-87. https://doi.org/10.1016/j.diabres.2009.03.005 PMid:19359063
18. American Diabetes Association. Screening for type 2 diabetes. Diabetes Care. 2003;26(Suppl 1):S21-4. https://doi.org/10.2337/diacare.26.2007.S21 PMid: 12502615
19. Liu S, Cui F, Ning K, et al. Role of irisin in physiology and pathology. Front Endocrinol (Lausanne). 2022;13:962968. https://doi.org/10.3389/fendo.2022.962968 PMid: 36225200 PMCid:PMC9549367
20. Guo Q, Cao S, Wang X. Betatrophin and insulin resistance. Metabolites. 2022;12(10):925. https://doi.org/10.3390/metabo12100925 PMid:36295827 PMCid:PMC9610572
21. Chaudhary I, Prasad S V, Y P G, et al. A comparative analysis of serum irisin levels and body composition indices in women with and without polycystic ovary syndrome (PCOS). Cureus. 2024;16(10):e71426. https://doi.org/10.7759/cureus.71426
22. Abdullateef HW, Al-Khateeb SM, Al-Maini EH. Simultaneous determination and association between serum levels of irisin and chemerin in PCOS. J Pak Med Assoc. 2024;74(10 (Supple-8)):S60-6. https://doi.org/10.47391/JPMA-BAGH-16-15 PMid:39434274
23. Majeed AA, Al-Qaisi AHJ, Ahmed WA. The comparison of irisin, subfatin, and adropin in normal-weight and obese polycystic ovary syndrome patients. Iran J Med Sci. 2024;49(6):350-8.
24. Pu D, Li L, Yin J, et al. Circulating ANGPTL8 is associated with the presence of metabolic syndrome and insulin resistance in polycystic ovary syndrome young women. Mediators Inflamm. 2019;2019:6321427. https://doi.org/10.1155/2019/6321427 PMid:31346314 PMCid:PMC6620840
25. Kahraman S, Altinova AE, Yalcin MM, et al. Association of serum betatrophin with fibroblast growth factor-21 in women with polycystic ovary syndrome. J Endocrinol Invest. 2018;41(9):1069-74. https://doi.org/10.1007/s40618-018-0831-2 PMid:29363048
26. Keikha F, Shahrokh Tehraninejad E, et al. The association of the betatrophin level with metabolic and inflammatory parameters in infertile women with polycystic ovary syndrome: A case-control study. Int J Reprod Biomed. 2022;20(1):29-36. https://doi.org/10.18502/ijrm.v20i1.10406 PMid:35308327 PMCid:PMC8902796

27. Eksi Haydardedeoglu F, Bagir GS, Haydardedeoglu B, et al. Serum betatrophin levels are reduced in patients with full-blown polycystic ovary syndrome. Gynecol Endocrinol. 2019;35(3):224-7. https://doi.org/10.1080/09513590.2018.1519791 PMid:30241452

28. Erbag G, Eroglu M, Turkon H, et al. Relationship between betatrophin levels and metabolic parameters in patients with polycystic ovary syndrome. Cell Mol Biol (Noisy-le-grand). 2016;62(5):20-4. PMid:27188865