Original Article

# Assessment of Irisin and Nesfatin-1 Levels in Non-Obese and Obese Women with Polycystic Ovarian Syndrome

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## Abstract

**Background:** In the developed world, some of the most common ovarian disorders include polycystic ovarian syndrome (PCOS), ovulatory dysfunction, hyperandrogenism, and polycystic ovaries which are the most characteristic in this woman endocrinopathy. It is associated with hyperinsulinemia and metabolic disorder. **Objective:** To estimate irisin, nesfatin-,1 and other biochemical parameters in obese and non-obese women with PCOS. **Materials and Methods:** The study comprised 90 women aged between 18 and 40 years, divided into two sub-groups. The first group consisted of 45 obese women with PCOS, and the second group consisted of 45 non-obese women with PCOS. Smokers, women with hypertension, or women consuming oral contraceptives were excluded from the groups. To determine whether the women were obese or not, body mass index was used. **Results:** The results of the study revealed that obese women with PCOS showed significantly higher levels of BMI, irisin, nesfatin-1, insulin, fasting glucose, and HOMA-IR compared to non-obese women ($P \leq 0.05$). However, no significant differences were found in LH, FSH, LH/FSH ratio, and total testosterone between the groups ($P < 0.05$). **Conclusion:** Irisin and nesfatin-1 levels surged in women with PCOS make them critical biomarkers in the progress of PCOS in obese and non-obese women.

**Keywords:** Enzyme-linked immunosorbent assay, IR, Irisin, Nesfatin-1, PCOS

## Introduction

In the developed world, one of the most common ovarian disorders is polycystic ovarian syndrome (PCOS), which is characterized by an excess of androgen that leads to the ovaries producing tiny sacs filled with fluid. This syndrome affects both the physiology and psychology of women, causing a lower quality of life throughout the reproductive years. High blood pressure and diabetes are two other diseases associated with PCOS due to various causes, including unbalanced eating habits, unhealthy lifestyles, and delayed diagnosis.[1]

Irisin is the new cytokine discovered in 2012 by Bostrom. Irisin is released from skeletal muscle through physical activity, adrenergic stimulation, and exposure to cold settings. The precursor of irisin is fibronectin type III domain containing 5.[2]

Irisin inhibits gluconeogenesis, fat formation, and lipid accumulation and plays a role in energy expenditure, absorption of glucose, glycogenolysis, and it may improve insulin sensitivity and homeostasis of glucose. Therefore, irisin is a possible target for treating metabolic disorders due to its beneficial effects on metabolism.[3]

The precursor protein for the peptide nesfatin-1 is nucleobindin 2 (NUCB2), a polypeptide of 82-amino acid. The peptides nesfatin-2 and nesfatin-3 are produced from NUCB2, though their roles are not yet assigned. Nesfatin-1, the 29-amino acid mid-fragment (nesfatin-130-59), possesses anorexigenic effects.[4]

Nesfatin-1 is mainly expressed in the pituitary, pancreas, adipose tissue, and digestive tract after being identified in the central nervous system as the cerebral cortex and

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hypothalamus. Nesfatin-1 and its binding sites are also expressed in the reproductive organs of both men and women.[5]

In addition, nesfatin-1 serves as a regulator for blood pressure, glucose homeostasis, gastrointestinal motility, stress, and reproduction. Through an increase in $Ca^{+2}$ flow via L-type channels, nesfatin-1 interacts with G-coupled receptor and facilitates glucose-induced insulin production. Moreover, by decreasing the quantity of meals, nesfatin-1 induces anorexia.[6]

Hormonal imbalances in progesterone, testosterone, gonadotropin-releasing hormone (GnRH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) play a major role in the onset and progression of PCOS, while normal physiology of the woman reproductive cycle is impacted, either directly or indirectly, by impaired in these hormone levels.[7,8]

The adenohypophysis secretes excessive levels of LH and FSH due to the aberrant pulsatile hyperstimulation of the hypothalamus, resulting in the excessive release of GnRH.[7]

## Materials and Methods

This research was conducted as a cross-sectional study involving 90 women aged between 18 and 40 years, divided into two sub-groups. The first group consists of 45 obese women with PCOS, and the second group consists of 45 non-obese women with PCOS.

Medical history, family history, surgical history, and body mass index (BMI) were recorded for each PCOS woman.

A study was approved in the Babylon Teaching Hospital for maternity and children in Hilla City and private clinics between January and March 2024. An enzyme-linked immunosorbent assay was used to assess the concentrations of serum irisin, nesfatin-1, insulin, and total testosterone levels. FSH and LH were assessed using the Cobas e411 analyzer (Roche, Germany) and fasting blood glucose by spectrophotometric method. Statistical Package for the Social Sciences software (SPSS, IBM Corp., Chicago, IL, USA) was used for statistical analysis.

### Ethical approval

Before sample collection, all women participants were learned and allowed to verbally agreement. The college and hospital ethics committee were examined and approved the study procedure and subject information. They provide permission by the document number [IRB: 179, January 18, 2024].

### Statistical analysis

The results of the study were shown as mean ± standard deviation (SD). Student *t* test and the linear regression analysis were used for data evaluation. The confidence interval (CI) 95% and *P* value were used for data expression. SPSS (version 26) was performed. *P* value was considered significant at 0.05 or less.

## Results

The BMI has significantly surged in the obese women with PCOS group ($P \leq 0.05$) with a mean and SD of 32.56 ± 3.39 compared to the non-obese women with PCOS group with a mean and SD of 23.86 ± 1.91, as illustrated in Table 1.

The LH and FSH showed non-significant variation in the obese women with PCOS group at $P > 0.05$ with a mean and SD of 10.56 ± 3.29 and 5.51 ± 1.17 compared to the

**Table 1: BMI level in studied groups**

| Parameter | Group | No. | Mean ± SD | *P* value |
|---|---|---|---|---|
| BMI (kg/m²) | Obese | 45 | 32.56 ± 3.39 | <0.001 |
| | Non-obese | 45 | 23.86 ± 1.91 | |

**Table 2: Hormone concentration in studied group**

| Parameter | Group | No. | Mean ± SD | *P* value |
|---|---|---|---|---|
| LH (µIU/mL) | Obese | 45 | 10.56 ± 3.29 | 0.165 |
| | Non-obese | 45 | 9.12 ± 4.31 | |
| FSH (µIU/mL) | Obese | 45 | 5.51 ± 1.17 | 0.873 |
| | Non-obese | 45 | 5.45 ± 1.61 | |
| LH/FSH Ratio | Obese | 45 | 1.97 ± 0.65 | 0.471 |
| | Non-obese | 45 | 1.58 ± 0.62 | |
| Testosterone (nmol/L) | Obese | 45 | 6.61 ± 1.87 | 0.244 |
| | Non-obese | 45 | 5.89 ± 2.61 | |

non-obese women with PCOS group with a mean and SD of 9.12 ± 4.31 and 5.45 ± 1.61, respectively, as illustrated in Table 2.

The LH/FSH ratio was non-significantly differed in the obese women with PCOS group at $P > 0.05$ with a mean and SD of 1.97 ± 0.65 compared to the non-obese women with PCOS group with a mean and SD of 1.58 ± 0.62, as illustrated in Table 2.

There was a non-significant difference in total testosterone level in the obese women with PCOS group at $P > 0.05$ with a mean and SD of 6.61 ± 1.87 compared to the non-obese women with PCOS group with a mean and SD of 5.89 ± 2.61, as illustrated in Table 2.

Fasting blood glucose was significantly elevated in the obese women with PCOS group ($P \leq 0.05$) with a mean and SD of 95.48 ± 3.81 compared to the non-obese women with PCOS group with a mean and SD of 92.81 ± 2.27, as illustrated in Table 3.

Insulin level was significantly elevated in the obese women with PCOS group ($P \leq 0.05$) with a mean and SD of 9.09 ± 2.34 compared to the non-obese women with PCOS group with a mean and SD of 7.206 ± 1.08, as illustrated in Table 3.

There was significant surged in HOMA-IR in the obese women with PCOS group ($P \leq 0.05$) with a mean and SD of 2.14 ± 0.57 compared to the non-obese women with PCOS group with a mean and SD of 1.64 ± 0.24, as illustrated in Table 3.

Irisin level was elevated significantly in the obese women with PCOS group ($P \leq 0.05$) with a mean and SD of 13.46 ± 5.81 compared to the non-obese women with PCOS group with a mean and SD of 5.49 ± 1.11, as illustrated in Table 4.

There was a significant increase in nasfatin-1 concentration in the obese women with PCOS group ($P \leq 0.05$) with a mean and SD of 681.44 ± 186.49 compared to the non-obese women with PCOS group with a mean and SD of 529.58 ± 168.55, as illustrated in Table 5.

## Discussion

PCOS is the most predominant endocrine disorder that is, associated with hyperandrogenemia, infertility, and obesity.[9]

Insulin resistance, unhealthy lifestyles, and environmental factors are responsible for developing obesity in PCOS patients.

There are many possible causes for variations in LH and FSH levels between obese and non-obese PCOS patients, one of them might be PCOS heterogeneity.[10]

Hormone profiles differ significantly between PCOS patients. Weight status might influence the fluctuation in LH and FSH levels. As well as, genetic factors, insulin resistance, and hormone abnormalities might affect PCOS. Although obesity might worsen metabolic dysfunction and hormonal abnormalities associated with PCOS, it may not necessarily result in appreciable variations in LH and FSH levels when compared to non-obese patients with the illness.[10,11]

**Table 3: Fasting blood glucose and insulin level in studied group**

| Parameter | Group | No. | Mean ± SD | *P* value |
|---|---|---|---|---|
| Glucose (mg/dL) | Obese | 45 | 95.48 ± 3.81 | 0.003 |
| | Non-obese | 45 | 92.81 ± 2.27 | |
| Insulin (mIU/L) | Obese | 45 | 9.09 ± 2.34 | <0.001 |
| | Non-obese | 45 | 7.206 ± 1.08 | |
| HOMA-IR | Obese | 45 | 2.14 ± 0.57 | <0.001 |
| | Non-obese | 45 | 1.64 ± 0.24 | |

**Table 4: Irisin level in studied group**

| Parameter | Group | No. | Mean ± SD | *P* value |
|---|---|---|---|---|
| Irisin (ng/mL) | Obese | 45 | 13.46 ± 5.81 | <0.001 |
| | Non-obese | 45 | 5.49 ± 1.11 | |

**Table 5: Nasfatin-1 level in studied group**

| Parameter | Group | No. | Mean ± SD | *P* value |
|---|---|---|---|---|
| Nesfatin-1 (pg/mL) | Obese | 45 | 681.44 ± 186.49 | 0.002 |
| | Non-obese | 45 | 529.58 ± 168.55 | |

Besides, insulin resistance is a dominant characteristic of PCOS, particularly in obese women. Hormone levels and the hormonal abnormalities associated with PCOS can lead to insulin resistance.[12]

LH and FSH levels might be affected by weight status besides insulin resistance. Further than weight, age, the phase of the menstrual cycle, and any underlying medical disorders might affect LH and FSH levels.[13]

The menstrual cycle and the growth of follicles are essential processes for both LH and FSH hormonal imbalances, although the LH/FSH ratio can be affected by hormonal abnormalities in PCOS. In spite of weight status, obese and non-obese PCOS patients may show similar degrees of hormonal dysregulation, resulting in comparable LH/FSH ratios and insulin resistance.[8,10]

The non-significant variations in testosterone levels between obese and non-obese PCOS patients might be due to those with PCOS having insulin resistance, which raises testosterone levels irrespective of weight. Moreover, ovarian dysfunction can result in an excess of androgens (testosterone) produced by the ovaries, raising testosterone levels in both groups according to weight.[14]

Likewise, the manufacturing of testosterone can be facilitated by adipose tissue. Increased testosterone-to-estrogen conversion in adipose tissue, due to increased activity of aromatase enzyme, leads to variations in testosterone levels in obese persons.[15]

While irisin levels decline in obesity, it is essential to remember that, as Table 4 demonstrates, there may be some conditions in which irisin levels are elevated in obese PCOS patients than in non-obese PCOS patients. Several variables associated with the pathophysiology of obesity, and PCOS may be the cause of these phenomena. The main features of PCOS and obesity are insulin resistance. Compensatory mechanisms may activate insulin resistance.[16,17]

Hyperinsulinemia might result from severe insulin resistance in obese PCOS patients, as the body compensates for the reduction in insulin activity. Higher levels of insulin in obese people with PCOS might contribute to improved irisin synthesis. Insulin upregulates irisin expression, and obesity is an attendant to improved oxidative stress and chronic inflammation.[18,19] These statuses could lead to the production of inflammatory mediators like cytokines, affecting irisin levels. Higher irisin levels in obese PCOS patients may be a response to the inflammation caused by both obesity and inflammation accompanying with PCOS.[19]

Irisin levels can also be affected by hormonal irregularities associated with PCOS, like increased androgens and changes in estrogen levels. Androgens influence irisin expression, and these hormonal irregularities, in addition to obesity and PCOS, might result in elevated irisin production for metabolic processes.[12]

Nesfatin-1 is the peptide hormone; these adipokines play a role in energy balance, appetite, and metabolic processes. Nesfatin-1 levels are elevated in obese PCOS patients compared to non-obese.[20] These findings might be attributed to adipose tissue dysfunction and obesity, which cause structural and functional alterations in adipose tissue.[21]

As a compensation mechanism, obese people with PCOS release more nesfatin-1 for the hormonal imbalances and metabolic disruptions caused by dysfunctional adipose tissue.[20]

Furthermore, nesfatin-1 has been linked to the control of insulin sensitivity and glucose metabolism. Nesfatin-1 levels might be disturbed in insulin-resistant illnesses, including obesity and PCOS, due to compromised insulin signaling and glucose utilization. The presence of metabolic dysfunction and diminished insulin sensitivity in obese PCOS might be the cause of elevated nesfatin-1 levels.[22-24]

## Conclusion

This study proved that obesity has an effect on hormone levels besides insulin resistance in women with PCOS. Higher levels of irisin and nesfatin-1 in PCOS women play a vital role in PCOS pathogenesis.

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### Conflicts of interest

There are no conflicts of interest.

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