

DIAGNOSTIC AND PATHOGENETIC SIGNIFICANCE OF ADIPOKINES IN POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder associated with reproductive dysfunction, insulin resistance, obesity, and chronic inflammation. This study aimed to investigate the diagnostic and pathogenetic significance of adiponectin, leptin, resistin, and ghrelin in women with PCOS. A prospective comparative study included 180 women aged 18–40 years, comprising 100 patients with PCOS and 80 healthy controls. Serum adipokine levels were measured using enzyme-linked immunosorbent assay. Women with PCOS demonstrated decreased adiponectin and ghrelin levels and increased leptin and resistin concentrations. Adipokine abnormalities were associated with insulin resistance, obesity, and reproductive dysfunction. These findings suggest that adipokines may serve as additional biomarkers for PCOS assessment and treatment monitoring.

Keywords: Polycystic ovary syndrome; adipokines; adiponectin; leptin; resistin; ghrelin; insulin resistance; infertility; metabolic disorders; biomarkers.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine-metabolic disorders in women of reproductive age and occupies a leading position among causes of endocrine infertility [1,2]. According to current data, the prevalence of PCOS in the population ranges from 8% to 20%, depending on the diagnostic criteria used, including the Rotterdam, NIH, and AE-PCOS Society criteria [3,4]. The disorder is characterized by marked clinical and metabolic heterogeneity and is accompanied by ovulatory dysfunction, hyperandrogenism, insulin resistance, obesity, chronic inflammation, and an increased risk of cardiovascular complications [5,6]. Despite substantial progress in the study of PCOS, the mechanisms underlying its development remain insufficiently understood, and early diagnosis continues to represent a major clinical challenge.

In recent years, particular attention has been paid to the role of adipose tissue as an active endocrine organ involved in the regulation of reproductive function and metabolic homeostasis [7]. Adipose tissue synthesizes a wide range of biologically active substances—adipokines—among which adiponectin, leptin, resistin, and ghrelin are of greatest interest [8,9]. These proteins are involved in the regulation of energy metabolism, tissue insulin sensitivity, inflammatory responses, steroidogenesis, and functioning of the hypothalamic-pituitary-ovarian axis [10]. Dysregulated adipokine secretion is considered one of the key mechanisms underlying metabolic and reproductive disturbances in PCOS.

Adiponectin has pronounced insulin-sensitizing and anti-inflammatory properties, and reduced concentrations are associated with the development of insulin resistance and hyperandrogenism in patients with PCOS [11,12]. Leptin, a regulator of energy balance and reproductive function, is often found at elevated concentrations in PCOS, particularly in patients with obesity and metabolic syndrome [13]. Elevated resistin levels are associated with chronic subclinical inflammation and impaired carbohydrate metabolism characteristic of this syndrome [14]. At the same time, ghrelin, which participates in the regulation of appetite and energy metabolism, tends to be reduced in patients with PCOS according to various studies, which may reflect impaired mechanisms of metabolic adaptation [15].

Current studies indicate a close relationship between changes in adipokine levels and the clinical manifestations of PCOS, including anovulation, infertility, obesity, and insulin resistance [16,17]. However, findings across studies remain inconsistent, which may be related to ethnic characteristics of the populations examined, differences in PCOS phenotypes, patient age, and the presence of concomitant metabolic disorders [18]. Data on the role of adipokines in women from the Uzbek population are particularly limited, underscoring the need for further investigation of this issue.

One promising direction in modern gynecological endocrinology is the search for highly sensitive biochemical markers that enable early diagnosis of PCOS, prediction of disease course, and assessment of treatment efficacy [19]. Investigation of adipokine profile characteristics in patients with PCOS may contribute to a deeper understanding of the pathogenetic mechanisms of the disease and to improvement of diagnostic, therapeutic, and preventive approaches.

The aim of the present study was to investigate the diagnostic and pathogenetic role of adipokines (adiponectin, leptin, resistin, and ghrelin) in women with polycystic ovary



syndrome and to assess their relationships with the clinical and metabolic manifestations of the disease.

MATERIAL AND METHODS OF RESEARCH

Study Design

A prospective comparative clinical and laboratory study was conducted at the Department of Obstetrics and Gynecology and specialized gynecological units of the Republic of Uzbekistan from 2022 to 2025. The study focused on evaluating the diagnostic and pathogenetic role of adipokines in women with polycystic ovary syndrome (PCOS). All patients provided written informed voluntary consent to participate in the study and to the processing of personal data for scientific purposes. The study protocol complied with the principles of the World Medical Association Declaration of Helsinki (2013) and national ethical requirements for biomedical research.

Inclusion Criteria

- Women of reproductive age from 18 to 40 years.
- PCOS diagnosed according to the Rotterdam criteria (2003), with at least two of the following features: oligo- or anovulation; clinical and/or biochemical hyperandrogenism; ultrasound features of polycystic ovaries.
- No hormonal therapy for at least 3 months before inclusion in the study.
- Signed informed consent to participate in the study.

Exclusion Criteria

- Pregnancy and lactation.
- Type 1 or type 2 diabetes mellitus.
- Thyroid disorders, hyperprolactinemia, Cushing syndrome, and other endocrine disorders.
- Acute inflammatory diseases of the pelvic organs.
- Severe somatic diseases of the liver, kidneys, and cardiovascular system.
- Use of hormonal, anti-inflammatory, or metabolic medications within 3 months before the study.
- Incomplete clinical and laboratory data.

Group Formation

A total of 180 women were included in the study and divided into three groups:

Group 1 (n = 50) — patients with PCOS and infertility;

Group 2 (n = 50) — patients with PCOS without reproductive dysfunction;

Control group (n = 80) — apparently healthy women without clinical or ultrasound signs of PCOS.

Group comparability was assessed according to age, body mass index (BMI), disease duration, and major clinical characteristics.

Study Methods

All patients underwent a comprehensive clinical and laboratory assessment including medical history, evaluation of menstrual and reproductive function, anthropometric measurements, gynecological examination, and pelvic ultrasonography.

Ultrasonography was performed using an expert-class system with a 5–9 MHz transvaginal probe on days 5–7 of the menstrual cycle. Ovarian volume, antral follicle count, and stromal thickness were assessed.

To assess metabolic disturbances, fasting blood glucose and insulin levels were measured, and the HOMA-IR index of insulin resistance was calculated using the formula:

$$\text{HOMA-IR} = \text{fasting glucose} \times \text{fasting insulin} / 22.5$$

Serum concentrations of adiponectin, leptin, resistin, and ghrelin were measured by enzyme-linked immunosorbent assay (ELISA) using standard commercial kits according to the manufacturer's instructions. Blood samples were collected in the morning after an overnight fast on days 3–5 of the menstrual cycle.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics 26.0 (IBM, USA). Quantitative variables are presented as mean and standard deviation ($M \pm SD$). Normality of distribution was assessed using the Shapiro–Wilk test. Student's t-test or the Mann–Whitney U test was used to compare quantitative variables between groups. Correlation analysis was performed using Spearman's correlation coefficient. Differences were considered statistically significant at $p < 0.05$.

Laboratory and Clinical Examination Methods

Clinical and laboratory assessment of all patients was performed according to a uniform protocol. Complaints, menstrual and reproductive function, the presence of hirsutism, obesity, infertility, and metabolic disorders were evaluated. Anthropometric assessment included body mass index (BMI), waist circumference, and the waist-to-hip circumference ratio.

The degree of hirsutism was assessed using the modified Ferriman–Gallwey score. Pelvic ultrasonography was performed on days 5–7 of the menstrual cycle using a 5–9 MHz transvaginal probe. Ovarian volume, antral follicle count, stromal thickness, and the presence of ultrasound signs of polycystic ovarian morphology were assessed.

Laboratory Methods

Venous blood samples were collected in the morning after a 10–12-hour fast. Serum levels of glucose, insulin, total testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and concentrations of adiponectin, leptin, resistin, and ghrelin were measured.

Adipokine levels were measured by enzyme-linked immunosorbent assay (ELISA) using standard commercial test systems according to the manufacturers' instructions. Concentrations of the studied proteins were expressed in ng/mL and pg/mL.

The HOMA-IR index was calculated to assess insulin resistance:

$$\text{HOMA-IR} = \text{fasting glucose} \times \text{fasting insulin} / 22.5$$

A HOMA-IR value above 2.5 was considered indicative of insulin resistance.

Assessment of Treatment Efficacy

Patients with PCOS received comprehensive therapy including lifestyle modification, dietary therapy, and metformin at an individually selected dose. The duration of therapy was 6 months.

During treatment, clinical parameters, hormonal profile, and adipokine concentrations were reassessed. Particular attention was paid to changes in leptin, resistin, adiponectin, and ghrelin levels as potential markers of metabolic changes and treatment efficacy.

Results

The study included 180 women who met the inclusion and exclusion criteria. The main group consisted of 100 patients with polycystic ovary syndrome (PCOS), of whom 50 had infertility and 50 had preserved reproductive function. The control group consisted of 80 apparently healthy women of reproductive age. The groups were comparable in age and major anthropometric parameters (Table 1).

The mean age of patients in the main group was 27.4 ± 4.8 years and that of the control group was 26.9 ± 4.5 years ($t = 0.54$; $p = 0.58$). Body mass index (BMI) was statistically significantly higher in women with PCOS than in controls (29.1 ± 3.7 kg/m² vs 23.8 ± 2.9 kg/m²; $p < 0.05$). Most patients with PCOS had menstrual irregularities, signs of hyperandrogenism, and insulin resistance.

Parameter	PCOS with infertility (n=50)	PCOS without infertility (n=50)	Control (n=80)	p
Age, years (M $\pm$ SD)	27.8 ± 4.9	27.1 ± 4.6	26.9 ± 4.5	0.58
BMI, kg/m ²	29.6 ± 3.9	28.5 ± 3.4	23.8 ± 2.9	<0.05
HOMA-IR	3.8 ± 1.1	3.2 ± 0.9	1.9 ± 0.6	<0.05
Menstrual cycle disorder, n (%)	42 (84.0 %)	38 (76.0 %)	5 (6.3 %)	<0.001

Table 1. Clinical and metabolic characteristics of the examined women

Adipokine Levels

Analysis of serum adipokine concentrations revealed statistically significant differences between the groups (Table 2). Patients with PCOS had a significant reduction in adiponectin levels compared with the control group. The most pronounced decrease was observed in women with PCOS and infertility.

Leptin and resistin concentrations in the main group were significantly elevated relative to control values ($p < 0.05$). Elevated levels of these markers were more frequently recorded in patients with obesity and insulin resistance.

Ghrelin levels in women with PCOS tended to decrease, particularly in the subgroup of patients with infertility.

Parameter	PCOS with infertility	PCOS without infertility	Control	p
Adiponectin, μ g/mL	6.1 ± 1.8	7.4 ± 2.1	10.8 ± 2.5	<0.05
Leptin, ng/mL	31.5 ± 6.7	27.2 ± 5.9	14.6 ± 4.1	<0.05
Resistin, ng/mL	9.8 ± 2.3	8.7 ± 2.0	5.1 ± 1.4	<0.05
Ghrelin, pg/mL	412.5 ± 58.6	438.1 ± 61.2	502.4 ± 66.8	<0.05

Table 2. Adipokine levels in the examined patients

Correlation Analysis

Correlation analysis demonstrated a statistically significant negative association between patient age and ghrelin level:

$$r = -0.25; p < 0.05$$

These data indicate a tendency for ghrelin concentrations to decrease with age in patients with PCOS.

In addition, a moderate positive correlation was found between adiponectin and ghrelin levels:

$$r = 0.42; p < 0.05$$

This indicates a possible joint involvement of these adipokines in the regulation of energy metabolism and metabolic homeostasis.

Leptin and resistin levels positively correlated with body mass index and indices of insulin resistance (HOMA-IR), confirming their involvement in the development of metabolic disturbances in PCOS.

Assessment of Changes During Therapy

After comprehensive therapy with metformin, patients with PCOS showed favorable changes in the studied parameters. The most pronounced changes concerned leptin and resistin levels, whose concentrations decreased significantly compared with baseline values ($p < 0.05$).

At the same time, a moderate increase in ghrelin levels and a tendency toward normalization of adiponectin concentrations were observed, which may indicate improved energy metabolism and reduced severity of insulin resistance.

After therapy, a positive correlation between ghrelin and adiponectin levels persisted:

$$r = 0.49; p < 0.05$$

The obtained results confirm the involvement of adipokines in the pathogenesis of PCOS and indicate their potential use as additional diagnostic and prognostic biomarkers of the disease.

Overall Assessment of Results

Thus, patients with polycystic ovary syndrome demonstrated marked abnormalities in the adipokine profile, manifested by reduced adiponectin and ghrelin levels and increased leptin and resistin concentrations. These changes were closely associated with metabolic disturbances, insulin resistance, and reproductive dysfunction.

The obtained data confirm the systemic nature of PCOS and the important role of adipokines in the development of clinical and metabolic disturbances in this disorder.

RESULTS AND DISCUSSION

The present study demonstrated a significant role of adipokines in the pathogenesis of polycystic ovary syndrome (PCOS) and confirmed their diagnostic value in women of reproductive age. The results indicate marked abnormalities in the adipokine profile of patients with PCOS, characterized by reduced adiponectin and ghrelin levels and increased leptin and resistin concentrations compared with the control group.

The observed decrease in adiponectin levels is consistent with current concepts regarding its insulin-sensitizing and anti-inflammatory functions [1,2]. Adiponectin is known to increase tissue sensitivity to insulin, regulate lipid metabolism, and suppress chronic inflammation. Reduced adiponectin concentrations in patients with PCOS may be considered one of the key pathogenetic mechanisms underlying insulin resistance and metabolic disturbances [3].

Elevated leptin and resistin levels in the examined patients reflect the presence of chronic subclinical inflammation and disturbances in energy metabolism. Leptin, one of the major regulators of energy homeostasis, is frequently associated with obesity, hyperinsulinemia, and hyperandrogenism in PCOS [4]. Resistin, in turn, is considered a pro-inflammatory adipokine involved in the development of insulin resistance and endothelial

dysfunction [5]. Our findings of increased concentrations of these markers are consistent with several international studies and confirm the involvement of adipose tissue in the pathogenesis of PCOS.

Of particular interest is the observed decrease in ghrelin levels in patients with PCOS. Ghrelin participates in the regulation of appetite, energy metabolism, and function of the hypothalamic-pituitary-ovarian axis [6]. The identified negative correlation between patient age and ghrelin level:

$$r = -0.25; p < 0.05$$

may indicate progression of metabolic disturbances with increasing age in patients with PCOS. In addition, the identified positive correlation between adiponectin and ghrelin levels:

$$r = 0.42; p < 0.05$$

supports a possible functional interaction between these hormones in the regulation of energy balance and metabolic adaptation. Persistence of this relationship after therapy:

$$r = 0.49; p < 0.05$$

indicates a stable pattern of coordinated adipokine involvement in metabolic homeostasis.

Favorable changes during metformin therapy indicate the potential use of leptin and resistin levels as additional biochemical markers of treatment efficacy. Reduced concentrations of these adipokines may reflect a decrease in the severity of insulin resistance and chronic inflammation characteristic of PCOS.

The results of the present study are consistent with current international research on the role of adipokines in PCOS [7,8]. A distinctive feature of this study is the evaluation of the adipokine profile in women from the Uzbek population, which is important in view of the ethnic and metabolic characteristics of the region.

Study limitations include the relatively small patient sample, lack of long-term follow-up, and the limited range of biomarkers examined. In addition, genetic factors that may influence adipokine secretion and the clinical course of PCOS were not assessed.

A promising direction for future research is expanded investigation of the molecular genetic mechanisms underlying impaired adipokine secretion, as well as development of personalized diagnostic and therapeutic approaches that take into account the metabolic phenotype of patients with PCOS.

CONCLUSION

Patients with polycystic ovary syndrome demonstrated marked abnormalities in the adipokine profile, characterized by reduced adiponectin and ghrelin levels and increased leptin and resistin concentrations compared with apparently healthy women.

Changes in adipokine levels were closely associated with the development of metabolic disturbances, insulin resistance, and reproductive dysfunction in PCOS. The most pronounced changes were observed in patients with infertility and an elevated body mass index.

A statistically significant negative correlation was identified between patient age and ghrelin level:

$$r = -0.25; p < 0.05$$

indicating a tendency for ghrelin concentrations to decrease with age and a possible progression of metabolic disturbances in PCOS.

A moderate positive correlation was established between adiponectin and ghrelin levels:

$$r = 0.42; p < 0.05$$

which persisted after therapy:

$$r = 0.49; p < 0.05$$

confirming their coordinated involvement in the regulation of energy and metabolic homeostasis.

Metformin treatment was accompanied by reductions in leptin and resistin concentrations, which may indicate decreased severity of chronic inflammation and insulin resistance. These findings support consideration of these adipokines as potential biochemical markers of treatment efficacy in PCOS.

The study results confirm the important role of adipokines in the pathogenesis of polycystic ovary syndrome and support their potential use as additional diagnostic and prognostic markers for evaluating clinical and metabolic disturbances in patients with PCOS.

Investigation of the adipokine profile in women with PCOS represents a promising direction in modern gynecological endocrinology and may contribute to improvement of early diagnosis, prevention, and personalized treatment of this disorder.

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