CORRELATION OF LEPTIN AND ADIPONECTIN LEVELS WITH METABOLIC AND HORMONAL PROFILES IN PCOS PATIENTS: A COMPARATIVE STUDY WITH NORMAL CONTROLS

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ABSTRACT

Background: Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder characterized by metabolic and reproductive abnormalities, including insulin resistance and hyperandrogenism. Leptin and adiponectin, two adipokines involved in metabolic regulation, are known to be dysregulated in PCOS. This study aims to investigate the correlation between leptin and adiponectin levels and their association with metabolic and hormonal profiles in PCOS patients compared to healthy controls.

Methods: A prospective, observational study was conducted involving 120 women diagnosed with PCOS and 50 healthy controls. Leptin and adiponectin levels were measured using enzyme-linked immunosorbent assay (ELISA). The adiponectin-to-leptin ratio (ALR) was calculated, and correlations with BMI, LH/FSH ratio, and other metabolic parameters were analyzed. Data were analyzed using appropriate statistical methods.

Results: Leptin levels were significantly higher in the PCOS group compared to controls (25.34 ng/mL vs. 11.16 ng/mL, $p < 0.0001$), while adiponectin levels were significantly lower (2.93 mcg/mL vs. 21.44 mcg/mL, $p < 0.0001$). The adiponectin-to-leptin ratio was markedly reduced in PCOS patients (0.13 vs. 2.05, $p < 0.0001$). A significant correlation was observed between the adiponectin/leptin ratio and the LH/FSH ratio ($r = 0.2138$, $p = 0.019$).

Conclusion: This study highlights the dysregulation of leptin and adiponectin in PCOS, suggesting their potential role in metabolic and reproductive dysfunction. The adiponectin-to-leptin ratio emerges as a promising biomarker for insulin resistance and metabolic risk in PCOS patients.

Keywords: PCOS, leptin, adiponectin, insulin resistance, metabolic dysfunction, adiponectin-to-leptin ratio, reproductive hormones.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age, with a prevalence of 5-20% worldwide. It is characterized by chronic anovulation, hyperandrogenism, and polycystic ovaries on ultrasonography. While the exact etiology of PCOS remains elusive, it is considered a multifactorial condition influenced by genetic, environmental, and metabolic factors. The syndrome is associated with a variety of metabolic abnormalities, including insulin resistance, dyslipidemia, and increased risk of type 2 diabetes mellitus, which further complicates its management. Due to the metabolic and reproductive consequences, PCOS is increasingly being regarded as not merely a gynecological disorder but a systemic condition with significant long-term health risks.[1,2]

Leptin and adiponectin, two key adipokines, have emerged as crucial players in the metabolic regulation associated with PCOS. Leptin, a 16-kDa hormone primarily secreted by adipocytes, is involved in energy homeostasis, appetite regulation, and reproductive function. It acts on the hypothalamus to regulate food intake and energy expenditure and is believed to have a direct influence on gonadal function. Elevated leptin levels have been observed in obese individuals and are strongly associated with insulin resistance—a hallmark of PCOS. Conversely, adiponectin, another adipokine exclusively produced by adipose tissue, has anti-inflammatory, anti-atherogenic, and insulin-sensitizing properties. It enhances insulin sensitivity by promoting fatty acid oxidation and inhibiting hepatic glucose production. Unlike leptin, adiponectin levels are typically reduced in obesity and conditions characterized by insulin resistance, such as PCOS.[3,4,5]

The interplay between leptin and adiponectin is particularly intriguing in the context of PCOS, as both hormones have opposing roles in metabolic regulation. Elevated leptin levels combined with reduced adiponectin levels may exacerbate insulin resistance, thereby contributing to the

pathogenesis of PCOS. Furthermore, the leptin-to-adiponectin ratio has been proposed as a potential marker for insulin resistance and metabolic dysfunction in PCOS patients. However, the relationship between these adipokines and the hormonal profile in PCOS, including luteinizing hormone (LH), follicle-stimulating hormone (FSH), and anti-Müllerian hormone (AMH), remains underexplored.[6,7,8]

In this study, we aim to investigate the correlation between leptin and adiponectin levels and their association with metabolic and hormonal profiles in women with PCOS. By comparing these levels with those of healthy controls, this study seeks to elucidate the role of leptin and adiponectin in the pathophysiology of PCOS. Furthermore, this study will assess the potential utility of the adiponectin-to-leptin ratio as a biomarker for metabolic dysfunction in PCOS patients. Understanding the biochemical and hormonal correlations in PCOS can provide insight into its metabolic underpinnings and pave the way for targeted therapeutic strategies aimed at mitigating the long-term health risks associated with the syndrome.[9]

This comparative study, therefore, not only addresses the metabolic complications of PCOS but also explores the hormonal disturbances that could be influenced by adipokines, offering a more holistic understanding of this multifaceted disorder. By highlighting the correlation of leptin and adiponectin with metabolic and hormonal parameters, we aim to contribute to the growing body of research focused on improving the diagnosis, management, and prognosis of PCOS.

MATERIALS AND METHODS

Study Site: This study was conducted in the Department of Obstetrics and Gynecology at the Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), Varanasi, in collaboration with the Department of Zoology, BHU.

Study Population: The study included patients diagnosed with Polycystic Ovary Syndrome (PCOS) based on the Rotterdam criteria (2003), aged between 20 and 40 years. The control group consisted of women with regular menstrual cycles and at least two children.

Study Design:b This was a prospective, observational study.

Sample Size: The study involved 120 women diagnosed with PCOS and 50 control subjects.

Study Period: Data collection spanned from February 2022 to December 2024.

Inclusion Criteria

- **Cases**: Women aged 20-40 years diagnosed with PCOS based on the Rotterdam criteria.
- **Controls**: Women with regular menstrual cycles and at least two children.

Exclusion Criteria

- Age below 20 or above 40 years.
- Patients already diagnosed with and receiving medication for PCOS.
- Patients with known diabetes mellitus, hypertension, chronic liver disease, or any psychiatric disorder.

Data Collection: Following approval from the institutional ethics committee, detailed histories, clinical examinations, and laboratory evaluations were performed on all participants. The following variables were assessed:

1. **Laboratory Evaluations**:
    - Fasting and postprandial blood sugar levels.
    - Oral glucose tolerance test (OGTT) after 75g of glucose (2 hours).
    - Fasting lipid profile.
    - Hormonal profile: Anti-Müllerian hormone (AMH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (Day 2 of the menstrual cycle), leptin, and adiponectin levels.
    - Ultrasonography to assess the antral follicle count.
    - Thyroid profile.
2. **Blood Sample Collection**:
    - A 3 mL blood sample was collected in EDTA vials, centrifuged, and leptin and adiponectin levels were estimated using commercially available ELISA kits.

Leptin and Adiponectin Assay Procedures

- **Adiponectin Assay**: A solid-phase sandwich enzyme-linked immunosorbent assay (ELISA) was used to measure adiponectin levels. This assay utilizes a target-specific antibody precoated on a microplate to capture adiponectin. The intensity of the signal generated is proportional to the concentration of adiponectin in the sample.
    - **Assay Range**: 0.5-32 mcg/mL.
    - **Sensitivity**: 100 mcg/mL.
    - **Sample Type**: Plasma, serum, or supernatant (10 µL).
    - **Time-to-Result**: 3 hours and 20 minutes.

- **Leptin Assay**: A solid-phase sandwich ELISA was used to measure leptin levels. The assay detects leptin by capturing the target protein with precoated antibodies on a microplate, and the subsequent addition of a detection antibody creates a signal proportional to the leptin concentration.
    - **Assay Range**: 15.6-1000 ng/mL.
    - **Sensitivity**: <3.5 ng/mL.
    - **Sample Type**: Plasma, serum, or supernatant (10 µL).
    - **Time-to-Result**: 3 hours.

Statistical Analysis: All data were analyzed using appropriate statistical methods. Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. Parametric data were analyzed using the Student's t-test, while non-parametric data were assessed using the Mann-Whitney U-test. Categorical data were compared using Chi-square or Fisher's exact test where appropriate. Statistical significance was determined at a p-value of less than 0.05. Data analysis was performed using Microsoft Excel 2007 and SPSS (Version 22).

RESULTS

The study included 120 women diagnosed with Polycystic Ovary Syndrome (PCOS) and 50 healthy controls. The age distribution of the PCOS cases showed that the majority of the participants (96.57%) were between the ages of 21 and 30 years. Specifically, 40% were aged 21-25 years, and 56.57% were aged 26-30 years, with a mean age of 26.14 ± 2.24 years (Table 1).

Leptin and adiponectin levels demonstrated significant differences between the PCOS group and the control group. The mean leptin level in the PCOS group was 25.34 ng/mL (±5.99), compared to 11.16 ng/mL (±3.24) in the control group, yielding a highly significant T value of 15.76 ($p < 0.0001$). Adiponectin levels were significantly lower in the PCOS group, with a mean of 2.93 mcg/mL (±1.73), compared to 21.44 mcg/mL (±5.12) in controls (T value = 35.16, $p < 0.0001$). The adiponectin-to-leptin ratio was markedly lower in the PCOS group (0.13 ± 0.09) compared to the control group (2.05 ± 0.65), showing a T value of 31.85 ($p < 0.0001$) (Table 2).

In terms of biochemical changes, the mean luteinizing hormone (LH) level in the PCOS group was 10.86 ± 8.27 miU/mL, while the mean follicle-stimulating hormone (FSH) level was 6.59 ± 3.12 miU/mL, resulting in an LH/FSH ratio of 1.56 ± 0.94. The mean anti-Müllerian hormone (AMH) level was 15.02 ± 7.66 ng/mL, and the mean prolactin level was 17.40 ± 6.52 ng/mL (Table 3).

Correlation analysis between the adiponectin/leptin ratio and variables such as BMI, age, and the LH/FSH ratio revealed no significant correlation with BMI ($r = -0.066$, $p = 0.476$) or age ($r = -0.124$, $p = 0.176$). However, a significant correlation was observed with the LH/FSH ratio ($r = 0.2138$, $p = 0.019$) (Table 4).

TABLE 1: AGE DISTRIBUTION OF CASES

Age Group (Years)	Number of Cases (n = 120)	Percentage (%)
13-20	0	0.00
21-25	48	40.00
26-30	68	56.57
31-35	4	3.33
36-40	0	0.00
Total	120	100.00
Mean ± SD	**26.14 ± 2.24**	

TABLE 2: DISTRIBUTION OF ADIPONECTIN AND LEPTIN LEVELS IN CASES AND CONTROLS

Variable	Group	N	Mean	Std. Deviation	T value	P value
Leptin (ng/mL)	Cases	120	25.34	5.99	15.76	< 0.0001
	Controls	50	11.16	3.24		
Adiponectin (mcg/mL)	Cases	120	2.93	1.73	35.16	< 0.0001
	Controls	50	21.44	5.12		
Adiponectin/Leptin Ratio	Cases	120	0.13	0.09	31.85	< 0.0001
	Controls	50	2.05	0.65		

TABLE 3: DISTRIBUTION OF BIOCHEMICAL CHANGES IN CASES

Biochemical Parameter	Group	Mean ± SD
LH (miU/mL)	Cases	10.86 ± 8.27
FSH (miU/mL)	Cases	6.59 ± 3.12
AMH (ng/mL)	Cases	15.02 ± 7.66
Prolactin (ng/mL)	Cases	17.40 ± 6.52
LH/FSH Ratio	Cases	1.56 ± 0.94

TABLE 4: DISTRIBUTION OF ADIPONECTIN LEPTIN RATIO CORRELATION WITH VARIABLES IN CASES

Variable	Mean ± SD	Correlation Coefficient (r)	P value
Adiponectin/Leptin Ratio	0.13 ± 0.09		
BMI	23.16 ± 3.37	-0.066	0.476
Age	26.14 ± 2.24	-0.124	0.176
LH/FSH Ratio	1.56 ± 0.94	0.2138	0.019

DISCUSSION

The findings from this study highlight significant metabolic and hormonal disturbances in women with Polycystic Ovary Syndrome (PCOS) compared to healthy controls, particularly in the context of adipokine regulation. Leptin and adiponectin, two critical adipokines, showed marked differences between PCOS patients and controls, which aligns with existing literature indicating their pivotal role in insulin resistance and metabolic dysfunction associated with PCOS.

Our results demonstrated significantly elevated leptin levels in the PCOS group compared to the control group (25.34 ng/mL vs. 11.16 ng/mL), with a p-value of <0.0001. This is consistent with prior studies where leptin levels were elevated in PCOS patients, particularly those with higher body mass indices (BMIs). Leptin's role in energy regulation, appetite control, and its association with insulin resistance in obese individuals is well-documented. In PCOS, hyperleptinemia could contribute to the exacerbation of insulin resistance, as leptin resistance is known to impair glucose metabolism. However, the absence of significant correlation between leptin levels and BMI in this study suggests that leptin elevation may be influenced by factors beyond obesity, such as underlying hormonal imbalances in PCOS.[10,11]

Adiponectin, known for its insulin-sensitizing and anti-inflammatory properties, was significantly lower in the PCOS group compared to controls (2.93 mcg/mL vs. 21.44 mcg/mL, $p < 0.0001$). Reduced adiponectin levels in PCOS are widely recognized, particularly in women with insulin resistance. Given adiponectin's role in enhancing insulin sensitivity by promoting fatty acid oxidation and inhibiting hepatic glucose production, its deficiency in PCOS could be a key driver of the insulin resistance commonly seen in these patients. The results confirm the hypothesis that low adiponectin, alongside elevated leptin levels, may contribute to the metabolic dysregulation observed in PCOS.

The adiponectin-to-leptin ratio (ALR) has gained attention as a potential biomarker for insulin resistance, and our study further supports its relevance in PCOS. The ALR was significantly lower in the PCOS group compared to controls (0.13 vs. 2.05, $p < 0.0001$), underscoring the disproportionate imbalance between these two adipokines. The significant reduction in ALR suggests that this metric could serve as a valuable indicator of metabolic dysfunction in PCOS, as it reflects both elevated leptin and reduced adiponectin levels—two critical factors in insulin resistance.[12]

Regarding the hormonal profile, the LH/FSH ratio was significantly elevated in the PCOS group (1.56 ± 0.94), and we observed a positive correlation between the adiponectin/leptin ratio and the LH/FSH ratio ($r = 0.2138$, $p = 0.019$). This finding indicates a potential interplay between adipokines and reproductive hormones, particularly the hypothalamic-pituitary-gonadal axis. Hyperleptinemia has been associated with increased LH secretion, which could explain its correlation with the elevated LH/FSH ratio in PCOS patients.

Overall, this study confirms that the dysregulation of leptin and adiponectin in PCOS is closely associated with both metabolic and reproductive abnormalities. The adiponectin-to-leptin ratio, in particular, emerges as a potential biomarker for assessing insulin resistance and metabolic risk in PCOS patients. Further research should explore therapeutic interventions aimed at restoring the balance of adipokines to improve metabolic and reproductive outcomes in women with PCOS.

CONCLUSION

This study underscores the significant correlation between leptin and adiponectin levels and their association with metabolic and hormonal disturbances in women with PCOS. Elevated leptin levels and reduced adiponectin levels, alongside a lower adiponectin-to-leptin ratio, were strongly linked to insulin resistance and reproductive hormone imbalances in PCOS patients.

These findings highlight the potential role of the adiponectin-to-leptin ratio as a biomarker for metabolic dysfunction in PCOS, paving the way for future research into targeted therapeutic strategies.

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