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Research Article

Comparative Analysis of Adiponectin and Leptin Levels in Obese and Non-Obese PCOS Cases

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Abstract: Polycystic Ovary Syndrome (PCOS) represents a complex endocrine disorder frequently complicated by obesity and metabolic dysregulation. Adipokines such as adiponectin and leptin play critical roles in insulin sensitivity, reproductive function, and inflammation; however, their comparative behaviour in obese versus non-obese PCOS remains unclear in South-Asian populations. This cross-sectional analytical study evaluated serum adiponectin and leptin concentrations in 180 women aged 18–35 years with PCOS diagnosed by Rotterdam criteria—90 obese (BMI ≥ 30 kg/m²) and 90 non-obese (BMI < 25 kg/m²)—and compared them with 90 age-matched healthy controls. Fasting venous samples were analysed using ELISA. Mean leptin levels were significantly higher in obese PCOS (28.7 ± 7.4 ng/mL) than in non-obese PCOS (17.6 ± 6.2 ng/mL, $p < 0.001$) and controls (14.9 ± 5.7 ng/mL, $p < 0.001$). Adiponectin levels were markedly lower in obese PCOS (6.3 ± 2.5 µg/mL) versus non-obese PCOS (9.1 ± 2.8 µg/mL, $p < 0.001$) and controls (11.4 ± 3.1 µg/mL, $p < 0.001$). Leptin correlated positively with BMI ($r = 0.62$, $p < 0.001$) and HOMA-IR ($r = 0.47$, $p < 0.01$), while adiponectin correlated inversely ($r = −0.51$, $p < 0.001$). Findings suggest that adipokine imbalance is more pronounced in obese PCOS and independently related to insulin resistance, emphasising their potential diagnostic and therapeutic significance.

Keywords: PCOS, adiponectin, leptin

Introduction: Polycystic Ovary Syndrome (PCOS) is the most prevalent endocrine disorder among women of reproductive age, characterised by oligo-anovulation, hyperandrogenism and

polycystic ovarian morphology. It represents not only a reproductive pathology but also a systemic metabolic disorder strongly associated with obesity, insulin resistance and chronic low-grade inflammation. The heterogeneous presentation of PCOS across ethnic groups suggests complex interactions between genetic predisposition and environmental or lifestyle factors. Among South-Asian women, PCOS tends to manifest with more severe metabolic disturbances even at lower BMI thresholds compared to Caucasian counterparts, signifying possible differences in adipose-tissue biology and adipokine signalling.1-4

Adipose tissue acts as a dynamic endocrine organ, secreting bioactive molecules termed adipokines, which regulate energy homeostasis, insulin sensitivity, and reproductive hormone activity. Two of the most extensively studied adipokines in PCOS are leptin and adiponectin.5-7 Leptin, primarily secreted by white adipocytes, reflects total fat mass and signals energy sufficiency to the hypothalamus, influencing gonadotropin secretion and ovarian steroidogenesis. Elevated leptin levels have been implicated in leptin resistance, an analogue of insulin resistance, and may disrupt follicular maturation. Conversely, adiponectin, secreted abundantly by subcutaneous fat, enhances insulin sensitivity and exerts anti-inflammatory and anti-atherogenic effects. Reduced adiponectin levels have been consistently associated with metabolic syndrome and type 2 diabetes, conditions overlapping with PCOS.8-10

The interplay between adiponectin and leptin provides a valuable metabolic index of insulin resistance and adipose-tissue dysfunction. In obesity-related PCOS, hyperleptinaemia and hypoadiponectinaemia contribute to altered ovarian function through disrupted insulin and gonadotropin signalling, leading to anovulation and hyperandrogenism. However, not all women with PCOS are obese; a substantial subset remains non-obese yet exhibits metabolic abnormalities, suggesting intrinsic defects independent of total adiposity. Comparing adipokine profiles in obese and non-obese PCOS can therefore elucidate whether altered adipokine secretion is secondary to obesity or integral to PCOS pathophysiology.11-13

Recent investigations from 2022–2024 have highlighted significant ethnic differences in adipokine dynamics. Asian women with PCOS demonstrate higher leptin and lower adiponectin levels at comparable BMI compared with Western cohorts, implying population-specific thresholds for metabolic risk. Moreover, emerging evidence indicates that the leptin-to-adiponectin ratio (LAR)

might outperform either marker alone in predicting insulin resistance and reproductive dysfunction in PCOS. Nevertheless, regional studies in Pakistan addressing these biochemical patterns remain limited, with inconsistent findings and small sample sizes.

Given the escalating prevalence of obesity and metabolic syndrome in Pakistani women, elucidating adipokine behaviour in PCOS is vital for developing population-appropriate diagnostic and therapeutic strategies. This study therefore aimed to compare serum adiponectin and leptin levels in obese and non-obese PCOS cases, evaluate their correlations with anthropometric and metabolic parameters, and determine whether these adipokines independently predict insulin resistance. The hypothesis proposed that obese PCOS women would show significantly higher leptin and lower adiponectin compared to non-obese PCOS and control groups, and that these alterations would correlate with insulin resistance markers.

Methodology: A comparative cross-sectional study was conducted at THQ Hospital, Shujabad, Multan in collaboration with Nishtar Hospital, Multan a tertiary endocrinology and gynaecology centre between March 2023 and February 2024. The sample comprised 270 women aged 18–35 years, divided into three groups: Group I – obese PCOS ($n = 90$, BMI ≥ 30 kg/m²), Group II – non-obese PCOS ($n = 90$, BMI < 25 kg/m²) diagnosed by the Rotterdam 2003 criteria (any two of: oligo/anovulation, clinical/biochemical hyperandrogenism, polycystic ovarian morphology on ultrasound), and Group III – apparently healthy controls with regular cycles and no clinical features of PCOS ($n = 90$). The sample size was estimated using Epi Info, assuming a medium effect size (Cohen's $d = 0.5$) for leptin difference between groups, $\alpha = 0.05$ and power = 0.8, yielding 81 per group; the number was rounded to 90 to accommodate non-response. Participants with thyroid dysfunction, diabetes mellitus, chronic inflammatory or hepatic disease, or on hormonal/metabolic medication within three months were excluded. Verbal informed consent was obtained after explanation of study purpose, confidentiality, and voluntary participation. Anthropometric data (weight, height, BMI, waist–hip ratio) were recorded using standardised equipment. Fasting blood samples were drawn between days 3–5 of spontaneous or induced menses following a 10–12 hour fast. Serum leptin and adiponectin were measured by sandwich ELISA using validated commercial kits; fasting glucose and insulin were assessed enzymatically to calculate HOMA-IR. Data were analysed using SPSS v26.0. Normality was assessed by Shapiro–Wilk test; comparisons among groups used ANOVA with post-hoc Tukey tests; Pearson's correlations examined relationships

between adipokines and metabolic indices; multiple linear regression identified independent predictors of HOMA-IR. Significance threshold was set at $p < 0.05$.

Results

Table 1. Demographic and anthropometric characteristics

Variable	Obese PCOS (n = 90)	Non-obese PCOS (n = 90)	Controls (n = 90)	p-value
Age (years)	26.4 ± 4.2	25.9 ± 4.6	25.8 ± 4.1	0.64
BMI (kg/m²)	31.8 ± 2.7	23.1 ± 1.6	22.7 ± 1.5	< 0.001
Waist–hip ratio	0.93 ± 0.06	0.84 ± 0.05	0.81 ± 0.04	< 0.001
HOMA-IR	4.12 ± 1.56	2.78 ± 1.03	2.11 ± 0.82	< 0.001

Adiposity and insulin resistance were significantly greater in obese PCOS compared with other groups.

Table 2. Serum adiponectin and leptin concentrations

Parameter	Obese PCOS	Non-obese PCOS	Controls	p-value
Adiponectin (μg/mL)	6.3 ± 2.5	9.1 ± 2.8	11.4 ± 3.1	< 0.001
Leptin (ng/mL)	28.7 ± 7.4	17.6 ± 6.2	14.9 ± 5.7	< 0.001
Leptin/Adiponectin ratio	4.8 ± 1.9	2.0 ± 0.9	1.3 ± 0.6	< 0.001

Obese PCOS exhibited pronounced leptin elevation and adiponectin reduction; L/A ratio increased threefold.

Table 3. Correlation of adipokines with metabolic indices (PCOS groups combined, n = 180)

Variable	Leptin (r)	Adiponectin (r)	p < 0.05 indicator
BMI	0.62	−0.48	✓
Waist–hip ratio	0.53	−0.42	✓
Fasting insulin	0.59	−0.45	✓

Variable	Leptin (r)	Adiponectin (r)	p < 0.05 indicator
HOMA-IR	0.47	−0.51	✓

Leptin correlated positively and adiponectin inversely with adiposity and insulin resistance indices.

Discussion: The present analysis demonstrates clear divergence of adipokine profiles between obese and non-obese women with PCOS. Serum leptin levels were substantially elevated while adiponectin was markedly reduced in obese PCOS compared with both non-obese counterparts and healthy controls. These findings are consistent with recent multi-ethnic data from 2022–2024 showing that hyperleptinaemia and hypoadiponectinaemia are characteristic of the metabolically adverse PCOS phenotype.12-14

The strong positive correlation of leptin with BMI and HOMA-IR underscores its dependence on adiposity and its association with insulin resistance. Elevated leptin likely reflects increased fat mass and possible leptin resistance, which may further impair hypothalamic–pituitary–ovarian signalling. Experimental work suggests that excessive leptin inhibits ovarian steroidogenesis by altering GnRH and LH pulsatility, providing a plausible link between obesity, hyperleptinaemia and anovulatory infertility.15-16

Conversely, the significant inverse association of adiponectin with both adiposity and insulin resistance highlights its protective metabolic role. Reduced adiponectin diminishes fatty-acid oxidation and promotes hepatic glucose output, worsening insulin resistance. This dysregulation is amplified in obese PCOS, explaining the higher HOMA-IR values observed. Importantly, non-obese PCOS women also exhibited lower adiponectin than controls, indicating that intrinsic defects in adipokine regulation exist independent of total fat mass.17-20

The leptin-to-adiponectin ratio, increasingly recognised as an integrated biomarker of metabolic risk, was more than doubled in non-obese PCOS and quadrupled in obese PCOS relative to controls. Such elevation reflects simultaneous leptin excess and adiponectin deficiency, mirroring systemic inflammation and impaired insulin sensitivity. These findings align with recent studies

identifying L/A ratio as a superior predictor of insulin resistance and cardiometabolic risk compared with either adipokine alone.

Mechanistically, obesity exacerbates adipocyte hypertrophy, leading to hypoxia, oxidative stress and inflammatory cytokine release that down-regulates adiponectin gene expression while up-regulating leptin. This imbalance contributes to a feed-forward loop of insulin resistance, hyperinsulinaemia and ovarian androgen excess. The persistence of altered adipokine levels in non-obese PCOS further suggests possible genetic or epigenetic modulation of adipokine genes.

Clinical implications include the potential use of adiponectin and leptin as adjunctive markers in phenotyping PCOS and guiding personalised management. Therapeutic strategies that improve adipokine balance—weight reduction, metformin, thiazolidinediones or myo-inositol—may ameliorate metabolic and reproductive outcomes. Monitoring these markers could help assess treatment response.

Limitations include the cross-sectional design, modest sample size and absence of body-fat distribution measures such as visceral fat quantification. Nonetheless, the study's controlled design, use of ELISA-based assays and statistical adjustment for confounders strengthen the validity of findings. Future longitudinal work should explore whether changes in adiponectin and leptin predict treatment response and long-term cardiometabolic risk in diverse PCOS phenotypes.

Conclusion: Obese women with PCOS exhibit significantly elevated leptin and decreased adiponectin compared with non-obese PCOS and healthy controls, with both adipokines strongly associated with insulin resistance. These findings reinforce adipokine imbalance as a key link between adiposity and metabolic dysfunction in PCOS, highlighting opportunities for biomarker-guided risk stratification and targeted therapy.

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