

ORIGINAL ARTICLE

Evaluation Of Lipid Profile, and Preptin Between Obese Non-Diabetic Patients and Women with Polycystic Ovary Syndrome in Al Diwaniyah, Iraq

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Abstract

Background Obesity has been associated with polycystic ovarian syndrome (PCOS) since Stein and Leventhal first described it in 1935. When using equivalent diagnostic criteria. This implies that lifestyle variables like obesity cause PCOS. Obesity worsens PCOS-related reproductive and metabolic problems.

Materials and Method The present study included 40 women with polycystic ovarian syndrome at ages (17 -36) years, in addition, the study included 40 non-diabetic obese women with a mean age range of (18 -56) years, Between November 2022 and May 2023, the participants in this research were enrolled at Al-Diwanyah Teaching Hospital. All laboratory test analysis was completed at the Clinical Chemistry Research Lab and AL Diwaniyah Teaching Hospital, both located in the College of Medicine at the University of Al-Qadisiyah.

Results In the present results lipid profile, the mean cholesterol was significantly higher in the PCOS Group in comparison with the obese OND . There was no significant difference in the mean serum triglycerides, HDL, LDL, and VLDL between the PCOS Group and the OND group. There was no significant difference in the mean preptin level between the PCOS group and the obese OND ($p = 0.473$). Then there was a comparison of preptin levels before and after the treatment in OND patients there was a significant reduction in the level ($p < 0.001$), and in comparison of preptin levels before and after the treatment in PCOS patients there was a significant reduction in the level ($p < 0.001$).

Conclusion According to the current findings, treating overweight or obese PCOS patients with insulin resistance, the Homeostatic Model Assessment for Insulin Resistance, and metformin had comparable outcomes.

Keywords: PCOS; Obese OND; Preptin

1 Introduction

Polycystic ovary syndrome (PCOS) is a common endocrinopathy disorder that affects reproductive-aged women [1]; it becomes frequently manifest during early reproductive age [1]. It is a heterogeneous disorder

with multiple reproductive, cosmetic, and metabolic complexities characterized by dysfunction in ovulation clinical or biochemical hyperandrogenism and polycystic ovarian morphology [2]. It is the most common endocrine cause of infertility and increases the risk of ad-

verse pregnancy outcomes, metabolic syndrome, type 2 diabetes mellitus, and some carcinoma [3].

PCOS alters the normal menstrual cycle, which also makes it harder to become pregnant. In 70–80% of instances, women with PCOS experience reproductive problems [4]. This condition may also increase the likelihood of pregnancy issues. Women with PCOS are twice as likely to give birth prematurely than women without the condition. They also have an increased risk of gestational diabetes, hypertension, and miscarriage [5,6]. However, fertility therapies that enhance ovulation may help women with PCOS get pregnant. It is possible to increase the likelihood of a safe pregnancy by losing weight and controlling blood sugar levels [7,8].

The availability of metabolites that may influence insulin synthesis, metabolism, and peripheral action rises as abdominal adipose tissue bulk increases. Ovarian control involves insulin and the liver, adipose tissue, and muscles. Insulin stimulates steroidogenesis by interacting with insulin and insulin growth factor type I receptors in ovarian granulosa, thecal, and stromal cells. Insulin causes granulosa cells to increase their levels of 3-hydroxysteroid dehydrogenase, 17-hydroxylase, and 17-20 lyase activity. By increasing pituitary cell receptivity to luteinizing hormone (LH) receptor activation, insulin seems to enhance the ovarian steroidogenic response to gonadotropins further. Insulin may also inhibit the production of sex hormone-binding globulin (SHBG) in the liver and ovaries. The growth factor IGFBP-1 controls adrenal steroid synthesis, ovarian size, and the formation of cysts [9–12].

Preptin was first discovered in 2001 in rat experiments. It is a peptide hormone consisting of 34 amino acids which is secreted along with insulin from the pancreatic beta cells [13]. As an endocrine peptide, preptin is thought to activate the insulin-like growth factor receptor 2 (IGF2R), and as a result, induces calcium-dependent insulin secretion in association with protein C and phospholipase C when the glucose concentration is high [14]. In addition, preptin has insulin-like effects on bone metabolism, such as boosting cellular differentiation and affecting the functions of osteoblasts and osteoclasts [13]. Preptin plays a role in metabolic pathways. There is currently a very limited number of studies regarding preptin in patients with T2DM [15].

Preptin is another molecule thought to be effective in glucose metabolism. Preptin has 34 amino acids derived from pro-insulin-like growth factor II (pro-IGF-II) and is a new hormone of peptide structure known to play a role in mineral metabolism [16,17]. It is expressed from pancreatic beta cells together with insulin. An increase or decrease in the concentration of preptin levels in the circulation can correct insulin

expression, and therefore, it is thought to be an amplification of glucose-mediated insulin expression [18].

Metformin was proven to be short-term safe for both mother and child compared to insulin alone during pregnancy, but its long-term safety was not conclusively established [19]. Metformin has been demonstrated to be equally as effective and safe as insulin in the treatment of gestational diabetes in a number of observational studies and randomized controlled trials [20,21]. But there are a few red flags, and we don't know nearly enough to be particular about the drug's long-term safety for mom and baby. Metformin-treated pregnant women with GDM had lower rates of weight gain and preeclampsia compared to their insulin-treated counterparts [22,23]. Pregnant women on metformin had less visceral fat, which may lower the chance that their offspring may grow up with insulin resistance [24].

Metformin is a biguanide and an anti-hyperglycemic. It reduces appetite and calorie intake by reducing hepatic glucose production and increasing tissue sensitivity to insulin [25,26]. Metformin, marketed as Glucophage and other brand names, is the drug of choice for the initial treatment of type 2 diabetes, especially in overweight patients. Another use for it is in the management of polycystic ovary syndrome. It may be used orally with no adverse effects on weight. Antipsychotic patients may benefit from using this supplement off-label to lower their chances of developing metabolic syndrome [25,27].

The newborns of mothers who used metformin for gestational diabetes were smaller than those of mothers who took insulin. Children whose mothers used metformin during pregnancy had smaller birth weights, but by the time they reached the middle of childhood, they were more significant than those whose mothers took insulin. Long-term cardiometabolic illness has been linked to a pattern of low birth weight followed by catch-up growth that outpaces other children of the same age [28].

The most typical metformin side effects include mild, temporary, and often self-limiting stomach pain. These side effects may be lessened by starting with a low dose of metformin, increasing it gradually, and taking it with meals [29,30]. Metformin-induced lactic acidosis is an uncommon illness, but the chance of developing it may be decreased by following the precautions and contraindications that prevent the body from storing too much metformin or lactate. Metformin has become a popular treatment due to its many therapeutic advantages and absence of safety hazards when used with other ant-hyperglycemic medicines. Metformin is a well-known component for managing diabetes, as an immunotherapy for type 2 diabetes in its early stages, and as a supplement to almost all other

anti-hyperglycemic medications on the market today [31,32].

2 Material and method

2.1 Study Design

A case-control study was done on patients at Al-Diwanyah Teaching Hospital for this study.

2.1.1 Subjects

The present study included 40 women with polycystic ovarian syndrome with a mean age of 25.08 ± 5.21 years and an age range of (17 -36) years. In addition, the study included 40 non-diabetic obese women with a mean age of 25.80 ± 6.75 and a range of age of 25.80 ± 6.75 years and an age range of (18 -56) years, a mean of $29.80 \pm 4.12 \text{ kg/m}^2$ versus $30.58 \pm 5.80 \text{ kg/m}^2$, respectively and a range of $24 -41.5 \text{ kg/m}^2$ versus $25 -47.2 \text{ kg/m}^2$, respectively. Between November 2022 and May 2023, the participants in this research were enrolled at Al-Diwanyah Teaching Hospital. All laboratory test analysis was completed at the Clinical Chemistry Research Lab and AL Diwaniyah Teaching Hospital, both located in the College of Medicine at the University of Al-Qadisiyah. Each Subject completed an informed consent form in writing. Body weight (kg) divided by the square of height (meters) yields the body mass index (BMI).

2.1.2 Collection of the samples

Five milliliters of blood were drawn from each research group. Immediately after drawing 1 ml of blood, dipotassium-EDTA Vacutainer® tubes were filled. At room temperature, 37°C , the serum was centrifuged at (4000 rpm) for 15–20 minutes to separate it. To maintain the separated serum for biochemical examination at -20°C , Eppendorf tubes were used.

2.1.3 Kits

Table 1: Kits (Companies and Countries of Origin) used in the present study.

No	Kit	Company	Country
1	Cholesterol Kit	Biosystem	Spain
2	Cholesterol HDL Kit	Biosystem	Spain
3	Triglycerides Kit	Biosystem	Spain
4	Human Preptin ELISA Assay	Elabscience	USA

2.2 Biochemical analysis

2.2.1 Measurement of absorption the Cholesterol (Ch) by spectrophotometer

$$\text{Cholesterol (mg/dl)} = \frac{\Delta A \text{ sample } X \text{ concentration of standard } \Delta A}{\text{Standard}} \quad (1)$$

Where: n = 200 Standard Concentration of Tc (mg/dl of blood)

2.3 Measurement of absorption of the Triglycerides

2.3.1 Calculation

$$\text{Triglyceride (mg/dl)} = \frac{\Delta A \text{ sample } X \text{ concentration of standard } \Delta A}{\text{Standard}} \quad (2)$$

Where: n = 200 Standard Concentration of TG (mg/dl of blood)

2.4 Measurement of absorption of the High-Density Lipoprotein- Cholesterol by spectrophotometer

2.4.1 Calculation

The HDL Cholesterol concentration in the sample is calculated using the following general formula.

$$\text{HDL cholesterol (mg/dl)} = \frac{\Delta A \text{ sample } X \text{ concentration of standard } \Delta A}{\text{Standard}} \quad (3)$$

2.5 Measurement of absorption of the Low-Density Lipoprotein- Cholesterol

2.5.1 Calculation

$$[\text{Totalchol}] = [\text{VLDL} - \text{chol}] + [\text{LDL} - \text{chol}] + [\text{HDL} - \text{chol}] \quad (4)$$

LDL-cholesterol is calculated from measured values of total cholesterol, triglycerides and HDL cholesterol according to the relationship:

$$[\text{LDL} - \text{chol}] = [\text{totalchol}] - [\text{HDL} - \text{chol}] - [\text{VLDL} - \text{chol}] \quad (5)$$

where $[\text{TG}]/5$ is an estimate of VLDL-cholesterol and all values are expressed in mg/dL.

2.6 Human Human Preptin

This ELISA kit uses the Sandwich-ELISA principle. Catalog No : E-EL-H2665

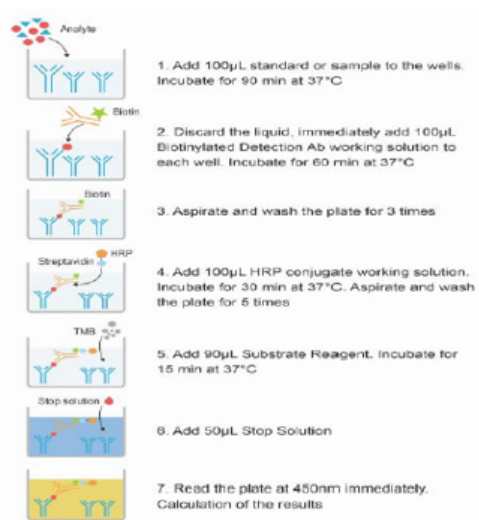


Figure 1: Assay procedure summary.

2.7 Statistical analysis

The means \pm standard deviation (SD) of data is provided. The Andersen-Darling test was employed to verify normality throughout the statistical analysis, which was conducted using SPSS Statistics 23. One-way ANOVA and post hoc analysis using Tukey's test

were used to evaluate whether differences between the groups were statistically significant. Throughout, a P value of 0.05 or less was regarded as significant.

3 Results

3.1 Comparison of mean age and mean baseline body mass index between obese non-diabetic patients and women with PCOS

Table 2 compares the median age and median baseline BMI of PCOS-positive women with obese non-diabetic individuals. 40 women with polycystic ovarian syndrome, with a mean age of 25.08 \pm 5.21 years and a range of 17 to 36 years, as well as 40 non-diabetic obese women, with a mean age of 25.80 \pm 6.75 years and a range of 18 to 56 years, were included in the current research. Between the PCOS group and the obese non-diabetic group, there was no discernible difference in mean age ($p = 0.327$). Additionally, there was no statistically significant difference in the mean body mass index (BMI) across study groups ($p = 0.493$); the ranges were 24 -41.5 kg/m² and 25 -47.2 kg/m², respectively, with a mean of 29.80 \pm 4.12 kg/m² and 30.58 \pm 5.80 kg/m² respectively.

Table 2: Comparison of mean age and mean baseline body mass index between obese non-diabetic patients and women with PCOS.

Characteristic	PCOS group $n = 40$	Obese non-diabetic group $n = 40$	p
Age (years)			
Mean \pm SD	25.08 \pm 5.21	25.80 \pm 6.75	0.327 I NS
Range	17 -36	18 -56	
BMI Before (kg/m ²)			
Mean \pm SD	29.80 \pm 4.12	30.58 \pm 5.80	0.493 I NS
Range	24 -41.5	25 -47.2	

SD: standard deviation; **n:** number of cases; **I:** independent samples t-test; **NS:** not significant; **BMI:** body mass index

3.2 Comparison of serum lipid profile between obese non-diabetic patients and women with PCOS

Table 3 compares the blood lipid profiles of obese non-diabetic individuals with PCOS-affected women. Comparing the PCOS group to the obese non-diabetic group, the mean cholesterol was considerably higher in the PCOS group, coming in at 182.51 \pm 37.35 mg/dl against 160.19 \pm 45.20 mg/dl, respectively ($p = 0.018$). Between the PCOS group and the obese non-diabetic group, the mean serum triglyceride was not significantly different (166.52 \pm 90.37 mg/dl vs 148.18 \pm 65.85 mg/dl, respectively; $p = 0.303$).

The mean serum HDL levels between the PCOS group and the obese non-diabetic group were 44.97 \pm 6.68 mg/dl and 43.75 \pm 10.42 mg/dl, respectively, with a p-value of 0.535 showing no difference between the two groups. Additionally, there was no statistically significant difference in mean serum LDL between the PCOS group and the obese non-diabetic group ($p = 0.298$), 92.09 \pm 26.49 mg/dl against 98.87 \pm 31.15 mg/dl, respectively. Additionally, the mean serum VLDL levels between the PCOS group and the obese non-diabetic group were 37.94 \pm 20.11 mg/dl against 32.67 \pm 17.97 mg/dl, respectively, with a p-value of 0.298 indicating no statistically significant difference.

Table 3: Comparison of serum lipid profile between obese non-diabetic patients and women with PCOS.

Characteristic	PCOS group <i>n</i> = 40	Obese non-diabetic group <i>n</i> = 40	p
Cholesterol (mg/dl)			
Mean ±SD	182.51 ±37.35	160.19 ±45.20	0.018 I *
Range	122 -276	12 -200	
Triglyceride (mg/dl)			
Mean ±SD	166.52 ±90.37	148.18 ±65.85	0.303 I
Range	18 -472	60 -280	NS
HDL (mg/dl)			
Mean ±SD	44.97 ±6.68	43.75 ±10.42	0.535 I
Range	30 -60	5.7 -63.6	NS
LDL (mg/dl)			
Mean ±SD	92.09 ±26.49	98.87 ±31.15	0.298 I
Range	28 -147.1	40.7 -165	NS
VLDL (mg/dl)			
Mean ±SD	37.94 ±20.11	32.67 ±17.97	0.220 I
Range	5.5 -100	10.3 -79.2	NS

HDL: high density lipoprotein; **LDL:** low density lipoprotein; **VLDL:** very low density lipoprotein; **I:** independent samples t-test; **SD:** standard deviation; **NS:** not significant; *****: significant at $p \leq 0.05$.

Table 4: Comparison of preptin level between obese non-diabetic patients and women with PCOS.

Characteristic	PCOS group <i>n</i> = 40	Obese non-diabetic group <i>n</i> = 40	p
Preptin Before treatment			
Medina (IQR)	90.85 (186.80)	87.85 (66.50)	0.473
Range	3.5 -200	3.4 -181.5	NS

Table 5: Comparison of preptin level before treatment and after treatment in obese non-diabetic patients.

Characteristic	Before treatment <i>n</i> = 40	After treatment <i>n</i> = 40	p
Preptin			
Medina (IQR)	87.85 (66.50)	57.15 (178.00)	<0.001 ***
Range	3.4 -181.5	3.6 -200	

IQR: inter-quartile range

3.3 Comparison of preptin level between obese non-diabetic patients and women with PCOS

Table 4 compares preptin levels between obese non-diabetic individuals and PCOS-affiliated women. The mean preptin level between the PCOS group and the obese non-diabetic group was 90.85 vs. 87.85, respectively ($p = 0.473$), with no statistically significant difference.

3.4 Comparison of preptin level before treatment and after treatment in obese non-diabetic patients

A comparison of preptin levels before treatment and after treatment in obese non-diabetic patients is shown

in Table 5. There was a significant reduction in the level from 87.85 (66.50) to 57.15 (178.00), ($p < 0.001$).

3.5 Comparison of preptin level before treatment and after treatment in PCOS

A comparison of preptin levels before treatment and after treatment in PCOS patients is shown in Table 6. There was a significant reduction in the level from 87.85 (66.50) to 57.15 (178.00), ($p < 0.001$).

Table 6: Comparison of Preptin level before treatment and after treatment in PCOS.

Characteristic	Before treatment n = 40	After treatment n = 40	p
Preptin			
Medina (IQR)	90.85 (186.80)	42.45 (96.52)	<0.001 W ***
Range	3.5 -200	3.4 -200	

W: Wilcoxon sign test; **IQR:** inter-quartile range

Table 7: Comparison of BMI before treatment and after treatment in obese non-diabetic patients.

Characteristic	Before treatment n = 40	After treatment n = 40	p
BMI (kg/m ²)			
Mean \pm SD	30.58 \pm 5.80	27.59 \pm 5.69	<0.001 Pa***
Range	24 -47.2	20 -43.5	

n: number of cases; **SD:** standard deviation; **BMI:** body mass index; **Pa:** paired t-test; ***: significant at $p \leq 0.001$

Table 8: Comparison of BMI before treatment and after treatment in PCOS.

Characteristic	Before treatment n = 40	After treatment n = 40	p
BMI Before (kg/m ²)			
Mean \pm SD	29.80 \pm 4.12	27.82 \pm 4.19	<0.001 Pa***
Range	24 -41.5	22.1 -39.7	

n: number of cases; **SD:** standard deviation; **BMI:** body mass index; **Pa:** paired t-test; ***: significant at $p \leq 0.001$

3.6 Comparison of BMI before treatment and after treatment in obese non-diabetic patients

A comparison of BMI before treatment and after treatment in obese non-diabetic patients is shown in Table 7. Treatment resulted in a significant reduction in mean body mass index in obese non-diabetic patients from 30.58 \pm 5.80 kg/m² to 27.59 \pm 5.69 kg/m² ($p < 0.001$).

3.7 Comparison of BMI before treatment and after treatment in PCOS

A comparison of BMI before treatment and after treatment in PCOS is shown in Table 8. Treatment resulted in a significant reduction in mean body mass index in PCOS patients from 30.58 \pm 5.80 kg/m² to 27.59 \pm 5.69 kg/m² ($p < 0.001$).

4 Discussion

Since the matching of ages is a need of such case-reference research, the absence of a significant varia-

tion in mean age in this study is a notable result. The non-significant difference in the mean BMI was due to the non-diabetic patients' selection for obesity and the majority of the PCOS group's female participants being overweight or obese. Numerous earlier publications have shown the connection between PCOS and obesity [33–36].

The majority agree that from an epidemiological and genetic perspective, PCOS and obesity are strongly associated in terms of the former. Obese or overweight women with PCOS range from 38 to 88% of the population. Gaining weight, particularly in early adulthood, is essential for the eventual development of PCOS, according to data from the Northern Finland Birth Cohort 1966. Furthermore, among obese women with PCOS, even a small (5%) weight decrease is associated with a better PCOS phenotypic profile (including reproductive, hyperandrogenic, and dysmetabolic features) [37].

There was evidence of dyslipidemia in the PCOS group due to their higher mean serum cholesterol compared to the obese non-diabetic group and the fact that several of these women had a cholesterol level over 200 mg/dl. Our results and those of many other studies [38–41] show that women with PCOS often suf-

fer from dyslipidemia. PCOS is often accompanied by dyslipidemia. Women with PCOS had 26 mg/dL higher TG levels than controls, 12 mg/dL higher LDL-C levels, 19 mg/dL higher non-HDL-C concentrations, and 6 mg/dL lower HDL-C concentrations [42].

In addition, women with PCOS had a greater prevalence of dyslipidemia than non-PCOS women [43], with some studies reporting rates of up to 50–70% [44, 45]. According to another research, the health of female reproduction has also been linked to dyslipidemia. In women undergoing assisted reproduction, serum lipid levels were related to clinical pregnancy, live birth, and miscarriage [46]. Previous research found that abnormal TC, TG, LDL-C, and HDL-C values were associated with a greater number of oocytes retrieved from women with PCOS who were undergoing unstimulated natural cycles [47]. High serum TC was also a risk factor for the success of assisted reproduction in PCOS individuals [48]. Therefore, testing for dyslipidemia may be relevant for PCOS-affected women undergoing fertility treatment to assess their cardiometabolic health and to forecast their chances of getting pregnant [38].

In the study of Mierzwicka et al. (2018) [49], The blood preptin levels of women with PCOS were found to be considerably greater than those of women without PCOS, although there were no statistically significant connections between preptin levels and metabolic and hormonal indicators. These results are at odds with our own, in which we found no statistically significant difference between the PCOS and control groups, although at a greater level in the latter. Metformin's capacity to improve insulin resistance is shown by its ability to lower preptin levels, which it did in both the obese non-diabetic patients and the PCOS patients in the research. Recent increases in obesity rates have prompted an intensive study of novel peptides implicated in the pathophysiology of metabolic diseases [50]. Preptin seems to be one of the new markers with the greatest importance for metabolic ailments. Patients with PCOS are more likely to develop metabolic issues such as insulin resistance (IR), poor glucose metabolism, dyslipidemia, abdominal obesity, and nonalcoholic fatty liver disease (NAFLD), particularly when they also have biochemical hyperandrogenism [51].

In line with our observation, Seifarh et al. in 2012 [52] found that metformin is an effective drug for reducing weight in a naturalistic outpatient setting in insulin-sensitive and insulin-resistant overweight and obese patients, Moreover, Guan et al. [53] their meta-analysis in 2020 found that Compared with control interventions, metformin appears to be an effective intervention for overweight women with PCOS.

5 Conclusion

According to the current findings, metformin and Preptin resistance all have comparable benefits when used to treat overweight or obese PCOS patients. Additionally, the current research supports the idea that metformin might be used as a preventative medication to reduce cardiovascular risk factors in hyperinsulinemic women with polycystic ovarian syndrome.

Conflict of interest: No conflicts of interest exist between the authors and the publication of this work.

Ethical consideration: The ethical committee approved the study at College of Medicine, University of Al-Qadisiyah, Al Diwaniyah, Iraq.

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