Annals of Clinical and Analytical Medicine
Original Research

Galanin-like peptide and leptin levels in polycystic ovary syndrome patients: A case-control study

Fehmi Unal[1], Osman Oğuz[2]
[1] Department of Obstetrics and Gynecology
[2] Department of Biochemistry, Istanbul Training and Research Hospital, Istanbul, Turkey

Abstract
Aim: In this study, we aimed to evaluate serum galanin-like peptide (GALP) and leptin levels in women diagnosed with polycystic ovary syndrome (PCOS) and to evaluate its relationship with obesity and insulin resistance.
Material and Methods: This study was conducted with 46 PCOS patients and 33 healthy women matched with a body mass index (BMI). Demographic characteristics of the patients [age, body mass index (BMI), number of births, menstrual characteristics, ovarian and endometrium characteristics], cholesterol, HOMA-IR, GALP, Leptin, AMH, FSH, LH, PRL, DHEA-SO4 and Testosterone levels were measured.
Results: A total of 79 individuals, 46 of whom (58.2%), with a mean age of 25.61 ± 7.15 years (14-43), were diagnosed with PCOS, and 33 of whom (41.8%) were in the healthy control group with similar features in terms of BMI, were included in our study. There was no difference between the groups in terms of GALP levels (3.4 vs. 5.5 ng/ml) (p=0.563). Leptin (10.2 vs. 4.5 ng / ml), AMH (7.3 vs. 2.6 ng / ml) and total testosterone (67.1 ± 25.12 vs. 40.1 ± 19.05 ng / dL) levels in the PCOS group were found to be higher than those in the control group (p<0.001).
Discussion: Our study showed that patients with PCOS had higher leptin and AMH levels than women in the healthy control group with similar BMI values, but there was no significant difference found between the two groups in terms of GALP levels.

Keywords
Galanin-Like Peptide, Leptin, Polycystic Ovary Syndrome

DOI: 10.4328/ACAM.20988 Received: 2021-12-10 Accepted: 2022-01-19 Published Online: 2022-01-25 Printed: 2022-05-01 Ann Clin Anal Med 2022;13(5):480-485
Corresponding Author: Fehmi Unal, Department of Obstetrics and Gynecology, Istanbul Training and Research Hospital, Istanbul, Turkey.
E-mail: unal.fehmi@gmail.com P: +90 533 770 43 96
Corresponding Author ORCID ID: https://orcid.org/0000-0002-8182-2051

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women of reproductive age with a prevalence of 6-25% [1]. The syndrome is associated with obesity, insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus (T2DM) and dyslipidemia [1,2].

Leptin is an adipokine, which affects oocyte maturation and activates ovarian enzymes involved in steroidogenesis, such as luteinizing hormone (LH) and follicle stimulation (FSH) [3].

The physiological relationship between leptin and GALP has been evaluated in several studies [4,5]. The presence of the leptin receptor in GALP-containing cells in the arcuate nucleus of rats and macaques has been demonstrated in morphological studies [5,6]. These observations showed that GALP can be regulated by a central and peripheral leptin-derived mechanism to control feeding behaviour. GALP levels are involved in nutritional regulation, and are thought to be associated with inflammation, sexual behaviour, and stress.

Although it has been shown that leptin levels are increased in non-obese patients with PCOS, there are not enough data on GALP levels [7]. The aim of this study was to evaluate serum leptin and GALP levels of patients with PCOS and to evaluate their relationship with metabolic parameters.

Material and Methods

Study population

A group of 46 PCOS and 33 healthy women with a matched body mass index (BMI) was included in our study. Patients were selected from the outpatient gynaecology clinics of our hospital. The control group patients had nonspecific complaints and had no pathological findings. Demographic information of the patients was recorded. Pelvic ultrasonography was performed and recorded in all cases.

Inclusion criteria

The diagnosis of PCOS was made according to the Rotterdam criteria [2]. Each patient's, Ferriman – Gallwey scores (FGS), height (cm), and weight (kg) were measured. BMI was calculated according to the following formula: BMI = body weight (kg) / height square (m2). Patients were defined as normal or underweight for those who were <25 kg/m2 and overweight for those ≥25 kg/m² based on WHO criteria. The FGS scores of 6 or higher were defined as hirsutism [8].

Exclusion criteria

All patients diagnosed with secondary etiologies of hyperandrogenism, diagnosed with chronic diseases, using any medications, smokers and those regularly consuming alcohol were excluded from the study.

Control Group

The control group consisted of healthy individuals with a FGS score <6, a regular menstrual cycles, normal androgen levels, a negative history for chronic diseases and normal ovaries in ultrasound examination. Smokers or alcohol users and patients taking any medications were excluded from the study.

Biochemical and hormonal tests

Venous blood samples were obtained at 9 am, between days 3-5 of the spontaneous or progesterone-induced menstrual cycle. Fasting plasma glucose (FPG), HDL, LDL and triglyceride levels were measured using spectrophotometric analyses (Beckman Coulter AU5800 (Beckman Coulter, CA) analyzer (Abbott Diagnostics, USA)). Fasting serum insulin (FSI), FSH, luteinizing hormone (LH), prolactin (PRL), dehydroepiandrosterone sulfate (DHEAS), total testosterone (TT), and thyroid-stimulating hormone (TSH) were measured immunoenzymatically (UniCelDxI800 analyzer (Beckman Coulter, CA)). The homeostatic Model Assessment for Insulin Resistance (HOMA-IR) was calculated using the following formula: HOMA-IR = Fasting blood glucose (mmol / L) x Fasting blood plasma insulin (mU / mL) / 22.5. Serum anti-Mullerian hormone (AMH) concentration was determined using an automated electrochemiluminescence immunoassay (ECLIA) and Roche-Cobas E411 (Roche Diagnostics, Germany).

Measurements of Leptin and GALP levels

After routine analysis, the separated serum was stored at -80°C for determination of GALP and leptin levels. Serum leptin levels were determined using the DRG-Leptin ELISA Kit® (DRG instruments-GmbH, Germany), a solid phase enzyme-linked immunosorbent assay based on the sandwich ELISA. The range in plasma leptin concentration levels was obtained according to the manufacturer's instructions. Serum GALP levels were measured by an enzyme-linked immunosorbent assay (Sandwich ELISA) using a commercially available matched Human Galanin-like Peptide Elisa Kit® (Bioassay Technology Lab, Shanghai, China). According to the manufacturer's specification, the assay range for GALP was 0.156-10 ng / ml and the mean sensitivity was 0.039 ng / ml, intra-assay precision was CV% <8% and inter-assay precision was CV% <10%, respectively. All measurements were done in pairs, and the average of the two measurements was taken into account. The ELISA method procedure was carried out according to the instructions provided by the manufacturer.

Statistical analysis

The SPSS 26.0 (IBM, New York, USA) program was used in the analysis of variables. The Kendall's tau-b test was used to examine the correlations of quantitative variables with each other. For the relationship between the classification of the cut-off value calculated according to the variables of the groups and the actual classification, sensitivity, specificity and accuracy rates were analyzed and expressed using ROC (Receiver Operating Curve) curve analysis. Logistic regression and neural network (Multilayer Perceptron-Radial Basis), two of the consulting machine learning methods, were used to find and predict the variable of greatest importance in the patient and healthy groups. The results of a Neural Network (Multilayer Perceptron) analysis, which is the most successful model among these methods, were used. Gradient descent was used for the optimization algorithm, hyperbolic tangent as the hidden layer activation function and exponential and softmax were used as the output layer activation function. Due to some missing data set, the training data set was set as 100%, while the Testing data set as 0%. Quantitative variables were expressed as mean ± SD (standard deviation) and median (Minimum / Maximum) in the tables, while categorical variables were shown as n (%). Variables were analyzed at a 95% confidence level, and a p-value of less than 0.05 was significant.

Ethical Consideration

Our study was approved by the Ethics Committee of the

hospital (Approval No:2194/21.02.2020). Informed consent was obtained from each patient and signed before the examination.

Results

A total of 79 individuals, 46 of whom (58.2%), with a mean age of 25.61 ± 7.15 years (14-43), were diagnosed with PCOS, and 33 of whom (41.8%) were in the control group with similar BMI, were included in our study. The average age of the control group was found to be higher than in the PCOS group (27 years vs. 21.5 years) (p<0.001) (Table 1). There was no difference between the groups in terms of GALP levels (3.4 ng/ml vs. 5.5 ng/ml) (p=0.563). Leptin (10.2 ng / ml vs. 4.5 ng / ml), AMH (7.3 ng / ml vs. 2.6 ng / ml), and total testosterone (67.1 ± 25.12 ng / dL vs. 40.1 ± 19.05 ng / dL) levels in the PCOS group were higher than those of the control group (p<0.001). While the HOMA-IR and fasting insulin levels of the patients in the PCOS group were found to be higher than those in the control group, the results of fasting blood glucose and cholesterol measurements were similar. FSH, LH and E2 levels were found to be higher in the control group than in the PCOS group (p=0.006, p=0.041 v p<0.001; respectively) (Table 1). TSH, DHEA-SO4 and PRL levels were similar in both groups. As expected, hirsutism and menstrual irregularity were found to most common complaints in the PCOS group (p<0.001).

A low level of negative correlation was found between GALP and age, BMI, fasting blood glucose and non-HDL cholesterol levels in the total patient and control groups. A low positive correlation was observed between leptin level and BMI, HOMA-IR, fasting insulin, total cholesterol level, non-HDL cholesterol level, LDL, triglyceride, TSH and T. testosterone. However, a low negative correlation was found between triglyceride and E2 levels and leptin (Table 2).

No significant difference was found between menstrual irregularity and BMI (<25, 25-30, >30 kg/m2) group distributions in terms of GALP and leptin levels in the control group. There was no significant difference in GALP and leptin levels in the PCOS group with menstrual irregularity, hirsutism, and morphological findings compatible with PCOS (p>0.05). However, patients with a BMI of <25 kg/m2 had a higher GALP value than patients with a BMI of 25-30 kg/m2 (p<0.001). The leptin level of the patients with a BMI of 25-30 25 kg/m2 was found to be higher than that of the patients with <25 v >30 kg/m2 (p<0.001).

When all participants were evaluated, it was found that women with menstrual irregularity, hirsutism and PCOS-compatible morphological findings had higher leptin levels and as BMI increased, leptin levels also increased. This status could not be shown for GALP (p>0.05).

The effect values for the change in GALP levels were determined to be age (57%), BMI (35%), non-HDL cholesterol (6%) and fasting blood glucose (4%), respectively. The effect values for the change in leptin levels were determined to be BMI (63%), non-HDL cholesterol (10%), HOMA-IR (8%) and triglyceride (5%) levels, respectively. In an analysis of those findings, which showed that they were significant for the diagnosis of PCOS in our study, testing with the Ensemble-learning Method found

Table 1. The table comparing the PCOS and control groups in the study

	Control (n=33) Median (Min-Max)	PCOS (n=46) Median (Min-Max)	P
Age (year)	27.0 (20-43)	21.5 (14-41)	<0.001 [u]
BMI (kg/m2)	24.5 (19.7-35.4)	24.0 (16-43)	0.939 [u]
GALP (ng/ml)	3.4 (0.2-23.3)	5.5 (0.5-24)	0.563 [u]
Leptin (ng/ml)	4.5 (0.1-18)	10.2 (1.2-25.2)	<0.001 [u]
AMH (ng/ml)	2.6 (0.2-8.7)	7.3 (0.8-30.8)	<0.001 [u]
HOMA-IR	1.4 (0.6 -17.6)	2.0 (0.7-9.9)	0.018 [u]
Insulin (mIU/L)	6.6 (2.6 -56.9)	9.5 (4-105)	0.035 [u]
Glucose (mg/dL)	90.0 (75.0 -125)	88.0 (7.8-144)	0.973 [u]
Total Cholesterol (mg/dL)	168.0 (129-300)	177.0 (123-352)	0.363 [u]
HDL (mg/dL)	54.0 (36-84)	51.0 (35.0-139)	0.402 [u]
Non-HDL (mg/dL)	114.0 (71-246)	123.0 (73.0-213)	0.246 [u]
LDL (mg/dL)	99.0 (59-228)	110.0 (62-201)	0.080 [u]
Triglyceride (mg/dL)	65.0 (34-258)	79.0 (34-324)	0.189 [u]
FSH (mIU/mL)	7.5 (2.7-35.4)	6.5 (2.3-10.4)	0.006 [u]
LH (mIU/mL)	9.9 (1.8-30.4)	6.3 (0.4-22)	0.041 [u]
DHEA-SO 4 (µg/dL)	233.9±106.53	256.9±131.15	0.478 [t]
Total Testosterone(ng/dL)	40.1±19.05	67.1±25.12	<0.001 [t]
	n (%)	**n (%)**	
Hirsutism			
No	33 (100) [B]	11 (23.9)	<0.001 [p]
Yes	0 (0)	35 (76.1) [A]	206.8 (11.7-3649.8) [OR]

[u] Mann Whitney u test(Monte Carlo), [t] Independent Samples t-test(Bootstrap), [p] Pearsons chi-Squared Test (Exact), SD.: Standard Deviation, OR Odds Ratio (95% Confidence interval), [A] Expresses significance compared to the control group, [B] Expresses significance compared to the control group. AMH: Anti-mullerian hormone; FSH: Follicle-stimulating hormone; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; GALP: Galanin-like peptide; BMI: Body mass index; LH: Luteinizing hormone; DHEA-SO4: Dehydroepiandrosterone sulfate, PCOS: Polycystic Ovarian Syndrome

Table 2. Correlation table with GALP and Leptin in the PCOS and control groups.

	Control (n=33)				Patient (n=46)				Patient vs Control	
	GALP (ng/ml)		Leptin(ng/ml)		GALP (ng/ml)		Leptin(ng/ml)		GALP (ng/ml)	Leptin
	r	P	r	P	r	P	r	P	p value *	p value *
GALP	1	-	-0.025	0.840	1	-	-0.158	0.123	-	0.572
IGF-1	-	-	-	-	0.121	0.281	-0.012	0.913	-	-
Age	-0.426	0.001	-0.064	0.608	-0.206	0.049	0.100	0.337	0.301	0.489
BMI	-0.009	0.943	0.248	0.056	-0.342	0.001	0.359	0.001	0.161	0.620
AMH	0.346	0.045	0.137	0.426	0.091	0.391	-0.293	0.006	0.373	0.146
HOMA-IR	0.047	0.709	0.399	0.001	-0.225	0.037	0.248	0.022	0.257	0.486
Insulin	0.068	0.577	0.419	0.001	-0.097	0.368	0.294	0.006	0.495	0.554
Glucose	-0.148	0.242	0.092	0.464	-0.232	0.032	0.067	0.536	0.721	0.917
Total Cholesterol	-0.243	0.049	0.363	0.003	-0.011	0.914	0.036	0.732	0.322	0.149
HDL	0.054	0.664	-0.186	0.132	0.097	0.352	-0.134	0.199	0.855	0.822
Non-HDL	-0.314	0.011	0.422	0.001	-0.086	0.485	0.296	0.016	0.355	0.574
LDL	-0.294	0.017	0.418	0.001	0.105	0.325	0.020	0.851	0.091	0.078
Triglyceride	-0.212	0.085	0.244	0.047	-0.032	0.754	0.138	0.183	0.445	0.644
FSH	-0.154	0.209	-0.140	0.251	0.053	0.673	-0.194	0.119	0.425	0.831
LH	0.119	0.329	-0.121	0.321	-0.155	0.221	-0.017	0.892	0.292	0.691
LH/FSH	0.210	0.085	-0.004	0.975	-0.254	0.045	0.052	0.683	0.047	0.814
DHEA-SO4	0.067	0.593	-0.004	0.974	-0.110	0.340	0.071	0.539	0.484	0.767
T. Testosterone	0.006	0.961	0.012	0.922	-0.172	0.147	0.094	0.426	0.483	0.747

Kendall's tau b Test, r: Correlation Coefficient; * Comparison of the correlations of patient and control groups with galanin and leptin; * Fisher Z transformation used AMH: Anti-mullerian hormone; FSH: Follicle-stimulating hormone; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; GALP: Galanin-like peptide; BMI: Body mass index; LH: Luteinizing hormone; DHEA-SO4: Dehydroepiandrosterone sulfate;

Table 3. Evaluation of the diagnostic success of GALP and Leptin levels with Ensemble-learning method

	Control (n=33)		PCOS (n=46)		Total (n=79)	
	GALP (DV)	Leptin (DV)	GALP (DV)	Leptin (DV)	GALP (DV)	Leptin (DV)
Independent Variable	Importance	Importance	Importance	Importance	Importance	Importance
Age	57.0%	-	17.0%	-	55.0%	-
BMI	-	-	70.0%	41.0%	35.0%	63.0%
AMH	13.0%	-	-	18.0%	-	-
HOMA-IR	-	5.0%	-	14.0%	-	8.0%
Insulin	-	5.0%	-	14.0%	-	3.0%
Glucose	-	-	5.0%	-	4.0%	-
Total Cholesterol	10.0%	22.0%	-	-	-	2.0%
Non-HDL	11.0%	33.0%	-	6.0%	6.0%	10.0%
LDL	9.0%	23.0%	-	-	-	4.0%
Triglyceride	-	12.0%	-	-	-	5.0%
FSH	-	-	-	-	-	1.0%
LH/FSH	-	-	3.0%	-	-	-
Total Testosterone	-	-	-	-	-	2.0%
Accuracy Ensemble Model / Reference Model	37.5 / 34.9	44.3 / 40.8	26.9 / 25.5	51.7 / 49.9	22.4 / 21.9	17.3 / 14.4

Ensemble-learning method: Bagging (Linear Regression); (Combining rule: Median); Model Selection method: Forward stepwise (Criteria: AICC); DV: Dependent Variable; AMH: Anti-mullerian hormone; FSH: Follicle-stimulating hormone; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; GALP: Galanin-like peptide; BMI: Body mass index; LH: Luteinizing hormone

that GALP levels were 22.4% and leptin levels were 17.3% (Table 3).

Discussion

We evaluated GALP and leptin levels in PCOS patients and their relationship with obesity and insulin resistance. In our study, patients with PCOS had higher AMH and leptin levels than those in the control group, but there was no significant difference between the GALP levels.

A history of weight gain is usually detected before the development of PCOS, and a healthy lifestyle change has been shown to reduce body weight and to lower testosterone in women with PCOS [9]. The prevalence of PCOS in obese women seeking help for weight loss is 28.3% [9]. However, in another study, PCOS prevalence was shown to be independent of obesity [10]. Parallel to this, most of the patients in our study were non-obese. In this respect, our study is notable in that it identified a higher rate of non-obese PCOS patients.

The pathophysiology underlying PCOS is not fully understood [11]. Previous studies have reported a higher prevalence of

obesity in PCOS patients compared to healthy women [12]. A recent study showed that an imbalance in adipokine secretion was not only associated with a higher likelihood of PCOS, but also with hyperandrogenism and increased ovarian follicle number. This result also suggests the role of adipokines in the different pathophysiological pathways of PCOS [13].

Many studies have suggested that HOMA-IR be used as a standard measure for diagnosing insulin resistance [14]. In our study, both groups had similar BMI values, and HOMA-IR levels were found to be higher in PCOS patients compared to control group.

Several studies found that leptin levels were higher than control groups of similar age. Opposite results were also published. The reason for this difference can be explained by the differences in the PCOS diagnostic criteria used to enroll the patients and the fact that PCOS patients with high leptin levels are also obese people. It was thought that obesity was the main reason for the increase in leptin levels, and that the leptin level has limited diagnostic discrimination in non-obese PCOS patients [12,15].

The putative role of GALP in regulating reproductive functions was thought to be a potential molecular link in the leptin/insulin and GnRH relationship to GALP [7,16,17]. In this sense, it has been postulated that reproductive dysfunction associated with diabetes is a defect in the function of GALP-expressing neurons [16]. It has been shown that more than 85% of GALP-containing neurons express leptin receptors and that leptin increases GALP mRNA expression in the hypothalamus [6,17]. Leptin inhibits the insulin-mediated stimulation of gonadotropin-induced ovarian steroidogenesis.

GALP elicits LH release following intracerebral injections in rats [16]. Moreover, GALP-induced LH secretion is blocked by the administration of the GnRH receptor antagonist in both rats and macaques; this suggests that GALP probably stimulates GnRH secretion through an intermediate cell [18,19]. This short-term effect of GALP in rats [16] appears to be similar in size to that of galanin and is thought to be due to GALP binding to galanin receptors [20,21]. Since GALP is found to be an important factor in the initiation of GnRH secretion and the regulation of LH secretion caused by GnRH, higher GALP levels are expected in patients with PCOS [7]. Increased LH release occurred following intracerebral injections of GALP in mice [16]. In addition, GALP has been shown to have a stimulating effect depending on estrogen [22]. As far as we know, only one study on GALP in patients with PCOS have been conducted yet [7]. Although Nyagolova et al. found higher GALP levels in PCOS patients, in our study, we could not find a significant difference between healthy women and PCOS patients regarding GALP levels.

When all the participants in our study were evaluated, women with menstrual irregularity, hirsutism, and PCOS-compatible morphological findings had higher leptin levels and as BMI increased, leptin levels also increased. We assume that GALP secretion disturbances may occur in PCOS subjects, however, we could not find similar results in reports that show a positive correlation of GALP levels with BMI, even though studies are still limited [23].

Some limitations of our study draw attention. PCOS group consisted of younger patients compared to similar studies, so it was thought that metabolic disorders may not have progressed sufficiently. In conclusion, we found that patients with PCOS had higher AMH and leptin levels than the control group with similar BMI values, but there was no significant difference between the two groups in terms of GALP levels.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: *None*

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Garvey WT, Mechanick JI, Brett EM, Garber AJ, Hurley DL, Jastreboff AM, et al. American association of clinical endocrinologists and American college of endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity: Executive summary. Endocr Pract. 2016;22(7):842–84.

2. No authors listed. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19-25.

3. Childs GV, Odle AK, MacNicol MC, MacNicol AM. The Importance of Leptin to Reproduction. Endocrinology. 2021;162(2):204.

4. Takenoya F, Hirako S, Wada N, Nonaka N, Hirabayashi T, Kageyama H, et al. Regulation of Feeding Behavior and Energy Metabolism by Galanin-like Peptide (GALP): A Novel Strategy to Fight Against Obesity. Curr Pharm Des. 2018;24(33):3926-33.

5. Cunningham MJ, Scarlett JM, Steiner RA. Cloning and distribution of galanin-like peptide mRNA in the hypothalamus and pituitary of the macaque. Endocrinology. 2002;143(3):755-63.

6. Takenoya F, Hirayama M, Kageyama H, Funahashi H, Kita T, Matsumoto H, et al. Neuronal interactions between galanin-like-peptide- and orexin- or melanin-concentrating hormone-containing neurons. Regul Pept. 2005;126(1-2):79-83.

7. Nyagolova PV, Mitkov MD, Orbetzova MM, Terzieva DD. Kisspeptin and galanin-like peptide (galp) levels in women with polycystic ovary syndrome. Int J Pharmaceut Med Res. 2016;4(5):7-12.

8. Matheson E, Bain J. Hirsutism in Women. Am Fam Physician. 2019;100(3):168-75.

9. Alvarez-Blasco F, Botella-Carretero JI, San Millán JL, Escobar-Morreale HF. Prevalence and characteristics of the polycystic ovary syndrome in overweight and obese women. Arch Intern Med. 2006;166(19):2081-6.

10. Yildiz BO, Knochenhauer ES, Azziz R. Impact of obesity on the risk for polycystic ovary syndrome. J Clin Endocrinol Metab. 2008;93(1):162-8.

11. Badawy A, Elnashar A. Treatment options for polycystic ovary syndrome. Int J Womens Health. 2011;3:25-35.

12. Pasquali R, Gambineri A, Pagotto U. The impact of obesity on reproduction in women with polycystic ovary syndrome. BJOG. 2006;113(10):1148-59.

13. Bicer M, Alarslan P, Guler A, Demir I, Aslanipour B, Calan M. Elevated circulating levels of secreted frizzled-related protein 4 in relation to insulin resistance and androgens in women with polycystic ovary syndrome. J Endocrinol Invest. 2020;43(3):305-313.

14. Bu Z, Kuok K, Meng J, Wang R, Xu B, Zhang H. The relationship between polycystic ovary syndrome, glucose tolerance status and serum preptin level. Reprod Biol Endocrinol. 2012;10:10.

15. Pehlivanov B, Mitcov M. Serum leptin levels correlate with clinical and biochemical indices of insulin resistance in women with polycystic ovary syndrome. Eur J Contraception Reprod Health Care. 2009;14:153–9.

16. Krasnow SM, Fraley GS, Schuh SM, Baumgartner JW, Clifton DK, Steiner RA. A Role for Galanin-Like Peptide in the Integration of Feeding, Body Weight Regulation, and Reproduction in the Mouse. Endocrinology. 2003;144(3):813–22.

17. Lawrence C, Fraley GS. Galanin-like peptide (GALP) is a hypothalamic regulator of energy homeostasis and reproduction. Front Neuroendocrinol. 2011;32(1):1-9.

18. Matsumoto H, Noguchi J, Takatsu Y, Horikoshi Y, Kumano S, Ohtaki T, et al. Stimulation Effect of Galanin-Like Peptide (GALP) on Luteinizing Hormone-Releasing Hormone-Mediated Luteinizing Hormone (LH) Secretion in Male Rats. Endocrinology. 2001;142(8):3693–6.

19. Cunningham MJ, Shahab M, Grove KL, Scarlett JM, Plant TM, Cameron JL, et al. Galanin-Like Peptide as a Possible Link between Metabolism and Reproduction

in the Macaque. J Clin Endocrinol Metab. 2004;89(4):1760–6.
20. Gundlach AL. Galanin/GALP and galanin receptors: role in central control of feeding, body weight/obesity and reproduction? Eur J Pharmacol. 2002;440(2-3):255-68.
21. Matsumoto Y, Watanabe T, Adachi Y, Itoh T, Ohtaki T, Onda H, et al. Galanin-like peptide stimulates food intake in the rat. Neurosci Lett. 2002;322(1):67-9.
22. Uenoyama Y, Tsukamura H, Kinoshita M, Yamada S, Iwata K, Pheng V, et al. Oestrogen-dependent stimulation of luteinising hormone release by galanin-like peptide in female rats. J Neuroendocrinol. 2008;20(5):626–31.
23. Fang P, Yu M, Gu X, Shi M, Zhu Y, Zhang Z, et al. Circulating galanin and galanin like peptide concentrations are correlated with increased triglyceride concentration in obese patients. Clin Chim Acta. 2016;461:126-9.

How to cite this article:
Fehmi Unal, Osman Oğuz. *Galanin-like peptide and leptin levels in polycystic ovary syndrome patients: A case-control study. Ann Clin Anal Med 2022;13(5):480-485*