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Galectin-1 as a potential diagnostic biomarker in polycystic ovary syndrome

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Abstract. – OBJECTIVE: This study was aimed at comparing the routine laboratory parameters and Galectin-1 levels of control and polycystic ovarian syndrome patients.

PATIENTS AND METHODS: 88 patients diagnosed with polycystic ovary syndrome and 88 healthy controls were considered for the study. Age groups of the patients ranged from 18 to 40. Serum TSH, Beta HCG, glucose, insulin, HOMA-IR, Hb1A1c, triglyceride, total cholesterol, LDL FSH, LH, E2, prolactin, testosterone, SHBG, DHESO4, HDL, Gal-1 levels were analyzed for each subject.

RESULTS: FSH, LH, LH/FSH, E2, prolactin, testosterone, SHBG, DHESO4, HDL and Gal-1 values of the subjects included in the study were statistically significantly different between the groups ($p<0.05$). Gal-1 and DHESO4 showed a strong positive connection ($p=0.05$). The sensitivity of Gal-1 level in PCOS patients was calculated as 0.997 and specificity as 0.716.

CONCLUSIONS: High levels of Gal-1 in PCOS patients suggest that it increases due to overexpression in response to inflammation.

Key Words:
Polycystic ovary syndrome, Gal-1, DHESO4, Diabetes, Inflammation, Obesity.

Abbreviations

PCOS: polycystic ovary syndrome; DHESO4: Dehydroepiandrosterone sulfate; SHBG: sex hormone-binding globulin; Gal-1: Galectin-1.

Introduction

One of the several endocrine illnesses, polycystic ovarian syndrome (PCOS), affects about one in every 15 women globally[1]. The prevalence of PCOS worldwide varies between 5% and 21% according to the NIH 1990 criteria, AE-PCOS 2006 criteria, and ESHRE/ASRM 2003 criteria[2]. There is hyperandrogenism, chronic ovulatory dysfunction, and polycystic-looking ovaries in this syndrome. In addition, various health complications such as obesity, cardiovascular diseases, metabolic syndrome, menstrual dysfunction, infertility, abnormal insulin activity, hair growth, and acne may be seen in patients with PCOS[3-5]. PCOS is associated with the elevation of inflammation markers of endothelin-1, visfatin, omentin, adiponectin, sensitive Interleukin 6 (IL-6), soluble intercellular adhesion molecule-1, tumor necrosis factor-alpha (TNF-α), soluble vascular cell adhesion molecule-1, asymmetric dimethylarginine, and plasminogen activator inhibitor-1 are all linked to the activation of the inflammatory cascade brought on by endothelial dysfunction and adipocyte hypertrophy[6-8]. There are studies[9,10] in which positive developments have been recorded regarding the regularization of menstrual cycles in patients with the endocrine disorder Polycystic Ovary Syndrome (PCOS), alpha lipoic acid and vitamin D supplementation in the treatment of infertility caused by ovulation problem, injection of embryo culture supernatant into the endometrial cavity and application of myo-inositol treatment.

According to the National Institutes of Health (NIH) 1990 Criteria, the presence of clinical or biochemical evidence of hyperandrogenism and chronic anovulation is necessary for the diagnosis of PCOS, while the presence of at least two of the findings of hyperandrogenism, oligomenorrhea,

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or amenorrhea and polycystic ovary appearance on ultrasound is required according to the 2003 Rotterdam Criteria. Hyperandrogenism is a diagnostic criterion of PCOS[11].

Galectins are lectins that bind β-galactoside carbohydrates *via* their carbohydrate recognition domains. All 15 identified mammalian galectins contain 1 or 2 carbohydrate-binding domains (CRDs) of approximately 130 amino acids, and this diversity implicates galectins in many functions, including regulation of the immune system[12]. According to their molecular makeup, galectins can be classified as "proto-type" (Gal-1) galectins, which have only one CRD, "tandem-repeat" (Gal-8 and 9) galectins, which have two different CRDs linked together by a short peptide, and "chimera type" (Gal-3) galectins, which have a CRD attached to a non-lectin N-terminal region that some members of the galectin family cause innate and adaptive immune cells, as well as synovial fibroblasts, to respond in an anti-inflammatory manner In contrast, others exhibit pro-inflammatory activity that enhances the innate and adaptive immune system[13].

Galectin-1 (Gal-1) is a protein with a molecular weight of about 14 kDa that can form homodimers and is highly synthesized by immune cells. Gal-1 has been identified in mammals, in organs such as the spleen, lymph nodes, prostate, placenta, lung, hepatoma, brain, heart, and in fibroblasts, macrophages, T and B cells, ovarian cells, endothelial cells, and dendritic cells[14]. Gal-1 regulates the function and death of a variety of immune cells in the peripheral and central immune systems, including T cells, macrophages, and activated B cells[15]. Gal-1 promotes the polarization of Th1 to Th2 and Th17 to Treg, inhibits the secretion of pro-inflammatory cytokines, and plays an immunosuppressive and anti-inflammatory role due to its pro-apoptotic effect on active lymphocytes[12,16,17]. Therefore, Gal-1 may be a new target for diseases with inflammation in their pathogenesis.

We sought to investigate the association between serum Gal-1 levels and PCOS risk as well as the impact of several endocrine characteristics of PCOS on Gal-1.

Patients and Methods

Study Plan and Participants

People who applied to Malatya Turgut Ozal University Training and Research Hospital Gynecology and Obstetrics Clinic between April 15, 2022, and November 01, 2022, were included in the study. The patient's medical history was taken, and age, height, weight, body mass index (BMI), and waist circumference were recorded. The diagnosis of PCOS was made considering the 2003 Rotterdam consensus criteria. The PCOS patient group consisted of those who met at least two requirements, such as oligo or anovulation, clinical and/or biochemical symptoms of hyperandrogenism, and the usual ultrasonographic finding (presence of 12 follicles with a diameter of 2-9 mm). The diagnosis of hirsutism was made using the Ferriman-Gallwey approach. If a patient's FG scores were lower than 8, they were deemed hairy[18].

Total testosterone (ND: 0.52-2.42 nmol/L), dehydroepiandrosterone sulfate (ND: 10-248 g/dL), and/or free androgen index (SAI 5%) serum concentrations above the normal range are all considered signs of hyperandrogenism in PCOS patients[19].

Patients with an irregular menstrual cycle, as well as those with other causes of androgen excess (such as Cushing's syndrome, hyperprolactinemia, congenital adrenal hyperplasia or other diseases of the adrenal gland, galactorrhea, and pregnancy), impaired glucose tolerance or Type 1/Type 2 diabetes, hypertension, hyperlipidemia, active or chronic liver or kidney failure, congestive heart failure, coronary artery disease, gestational diabetes mellitus, or a According to the 2003 study[2,11], 88 females between the ages of 18 and 40 who fulfilled all exclusion criteria were classified as "PCOS patients[20]".

Eighty-eight healthy women who had regular menstrual cycles, no health issues including hirsutism, acne, or hyperandrogenism, met the inclusion criteria; while, who did not have PCOS by the 2003 Rotterdam consensus criteria served as the control laboratory tests within the normal range, over 18 years old, in the appropriate age group and the same age group as PCOS cases, and of same ethnicity and demographics were included. All people included in the study were informed about it, and their consent was obtained.

Glucose, triglycerides, total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels of participants (ARCHITECT, Toshiba, Abbott Park, IL, USA), HbA1c values ADAMS A1C, Arkray, Shiga, Japan), FSH, LH, E2, TSH, prolactin, BetaHCG, testosterone, SHBG, DHESO4 and insulin hormone values Roche Diagnostics Cobas E601, Tokyo, Japan), glucose, triglyceride, total cholesterol,

low-density lipoprotein (LDL), and high-density lipoprotein (HDL) readings (ARCHITECT, Toshiba, Abbott Park, IL, USA) were logged.

How to Get Serum Samples

The subjects who participated in the study had their blood drawn between days three and five of their menstrual cycle, during the early follicular phase. After an overnight fast (in the case of fasting between 20:00 after supper and 08:00 in the morning), blood samples were collected from the subjects (PCOS patients and healthy controls) in the morning and placed in a tube with a gel separator. Serum tubes were incubated at room temperature for 30 minutes and then centrifuged at 1200 g for 10 minutes. Serum samples were transferred to microvolume Eppendorf tubes and stored at -80°C until analysis.

Determination of Gal-1 Levels by ELISA Method

Galectin-1 levels were measured using a commercial Enzyme-Linked Immuno Sorbent Assay kit in accordance with kit instructions (Bioassay Technology Lab., Zhejiang, China). Using a microplate reader set to read at 450 nm wavelength, the samples' absorbance was calculated. The minimum detectable amount was 0.15 ng/mL, while the measurement range was 0.3-90 ng/mL.

Statistical Analysis

The statistical application SPSS 25 (Statistical Program in Social Sciences; IBM Corp., Armonk, NY, USA) was used to analyze the research's data. To determine if it adheres to the normal distribution, the Kolmogorov-Smirnov test was utilized[21]. For comparison tests, the significance threshold (p) was set at 0.05. The analysis used parametric test methods because the variables did not have a normal distribution ($p>0.05$). Since normality was not assumed, comparisons between independent paired groups were done using the Mann-Whitney U test. Cross tables were made for categorical data analysis, and Chi-square analysis was carried out. The binary logistic regression model was established to determine the distinguishing values between groups in case the dependent variable is categorical. The cut-off point was established using ROC analysis[22].

Results

Demographic Characteristics of PCOS Patients and Healthy Control Group

The results of the test to determine whether there was a difference between the groups based on the variables of marital status, age, and BMI of the study's participants are shown in the table below. According to the study participants' age, marital status, and BMI data, there was no statistically significant difference between the patient and control groups ($p>0.05$, Table I).

Comparison of Laboratory Markers of PCOS Patients and Healthy Control Groups

Regarding the study participants' TSH, Beta HCG, glucose, insulin, HOMA-IR, Hb1A1c, triglyceride, total cholesterol, and LDL variables, there was no statistically significant difference between the groups ($p>0.05$, Table II). FSH, LH, LH/FSH, E2, prolactin, testosterone, SHBG, DHESO4, HDL, and Gal-1 characteristics were statistically different across the groups ($p<0.05$, Table II).

Table I. Comparison of groups by gender and age distribution.

Variable	Groups		PCOS	Control	Total	p-value
Marital Status	Single	n	39	16	55	0.001*
		%	44.30%	18.20%	31.30%	
	Married	n	49	72	121	
		%	55.70%	81.80%	68.80%	
Age	Mean ± SD		28.14 ± 4.31	29.44 ± 7	28.79 ± 5.83	0.361
	M (min-max)		28 (20-37)	29 (19-42)	28 (19-42)	
BMI	Mean ± SD		22.5 ± 2.35	22.1 ± 1.99	22.31 ± 2.18	0.281
	M (min-max)		22.66 (16.41-33.23)	22.04 (17.78-27.06)	22.45 (16.41-32.23)	

n; frequency, %; percent, SD; standard deviation, M; median, pa; chi-square test value (χ^2), pb; Mann-Whitney U Test Value.

Table II. Comparison of groups by variables.

Variable	PCOS (n = 88)		Control (n = 88)		
	Mean ± SD	M (min-max)	Mean ± SD	M (min-max)	*p*-value
FSH (mIU/mL)	5.83 ± 1.4	6 (1.32-8.6)	7.75 ± 2.27	7.42 (3.63-13.9)	**0.001***
LH (mIU/mL)	8.3 ± 4.9	6.87 (1.98-23.5)	5.91 ± 1.91	5.96 (2.45-9.81)	**0.002***
E2 (pg/mL)	45.64 ± 25.53	40.45 (5-151)	58.75 ± 33.88	51.04 (17.8-227)	**0.001***
TSH (mU/L)	1.65 ± 0.73	1.54 (0.31-4.15)	1.8 ± 0.99	1.57 (0.14-5.02)	0.665
Prolactin (ng/mL)	16.6 ± 6.55	16.25 (1.27-35.93)	14.31 ± 6.81	13.1 (2.36-36.1)	**0.006***
BetaHCG (mIU/mL)	0.25 ± 0.43	0.2 (0.1-4.25)	0.2 ± 0.07	0.2 (0.1-0.81)	0.992
Testosterone (ng/dL)	0.33 ± 0.17	0.32 (0.1-0.78)	0.24 ± 0.11	0.22 (0.1-0.55)	**0.001***
SHBG (nmol/L)	46.51 ± 16.57	46.4 (12.9-105)	54.69 ± 18.14	54.95 (14.5-99.5)	**0.003***
DHESO4 (ng/dL)	204.14 ± 74.57	187.5 (17-415)	177.02 ± 85.19	156 (40.1-411)	**0.003***
Glucose (ng/dL)	89.13 ± 6.97	89 (72-100)	90.86 ± 6.03	91 (74-100)	0.097
Insulin (uU/mL)	8.8 ± 2.36	8.8 (4.7-18.9)	8.54 ± 2.35	9.19 (2.17-12.6)	0.830
HOMAIR (mmol/L)	1.94 ± 0.55	1.95 (0.84-4.67)	1.92 ± 0.52	2.1 (0.51-2.49)	0.521
HbA1c (%)	5.34 ± 0.25	5.4 (4.6-5.7)	5.31 ± 0.23	5.3 (4.58-5.8)	0.184
Triglyceride (mg/dL)	92.22 ± 29.41	92 (35-177)	93.4 ± 28.92	93.5 (34-150)	0.704
T. Cholesterol (mg/dL)	154.32 ± 23	154.5 (106-200)	151.61 ± 30.56	153 (94-199)	0.614
LDL (mg/dL)	95.95 ± 16.04	97.45 (58-127)	90.76 ± 16.38	94.85 (41.8-119.5)	0.077
HDL (mg/dL)	50.41 ± 6.97	48.1 (40.3-74)	47.95 ± 6.65	47.35 (36.9-70.1)	**0.019***
Gal-1	18.34 ± 3.04	18.54 (12.40-23.81)	9.44 ± 1.49	9.49 (5.16-12.07)	**0.001***
LH/FSH	1.49 ± 0.91	1.18 (0.30-4.87)	0.82 ± 0.37	0.73 (0.27-2.00)	**0.001***

SD; standard deviation, M; median, pa; Chi-square test value (χ^2), *p*; Mann-Whitney U Test Value *$p < 0.05$; there is a statistically significant difference between the groups.

ROC Analysis

The areas under the curve determined for the variables of the study participants' TSH, Beta HCG, glucose, insulin, HOMA-IR, Hb1A1c, triglyceride, total cholesterol, and LDL were not statistically significant ($p>0.05$, Figure 1). There are no specific PCOS-related TSH, Beta HCG, glucose, insulin, HOMA-IR, Hb1A1c, triglyceride, total cholesterol, and LDL readings (Table III, Figure 1).

The areas under the curve calculated for the FSH, LH, LH/FSH, E2, prolactin, testosterone, SHBG, DHESO4, HDL, and Gal-1 variables were a statistically significant finding ($p<0.05$, Figure 1). FSH, LH, E2, prolactin, testosterone, SHBG, DHESO4, HDL, and Gal-1 values are distinctive for PCOS, and the cut-off values of the values are given in Table III and Figure 1.

Gal-1, the parameter with the highest AUC value, and FSH, the parameter with the lowest AUC value, were the other parameters. The cut-off point for the Gal-1 ROC analysis was 8.97 points, which is the point with the highest sensitivity and the lowest specificity. At this point, the scale's sensitivity was found to be 0.997, while its specificity was found to be 0.716. The LH/FSH ratio had the highest AUC value after Gal-1, and the ROC analysis led to the determination of the 1.01 cut-off point, which equates to the point with the highest sensitivity and lowest specificity. The LH/FSH ratio's specificity was 0.978 at this stage, while its sensitivity was 0.989 (Table IV, Figure 1).

Table III. Comparison of Gal-1 and laboratory variables.

Points	Gal-1	
Value	r	*p*
FSH	0.005	0.964
LH	-0.054	0.619
E2	-0.132	0.222
TSH	0.023	0.831
Prolactin	-0.078	0.472
BetaHCG	0.001	0.992
Testosterone	-0.033	0.757
SHBG	-0.205	0.055
DHESO4	**0.218**	**0.042***
Glucose	0.122	0.258
Insulin	-0.021	0.845
HOMA-IR	0.017	0.876
HbA1c	0.176	0.102
Triglyceride	0.06	0.576
T. Cholesterol	-0.161	0.134
LDL	-0.196	0.067
HDL	-0.085	0.432
LH/FSH	-0.031	0.777

r; Spearman's rank correlation coefficient, *$p < 0.05$; there is a statistically significant relationship between the variables.

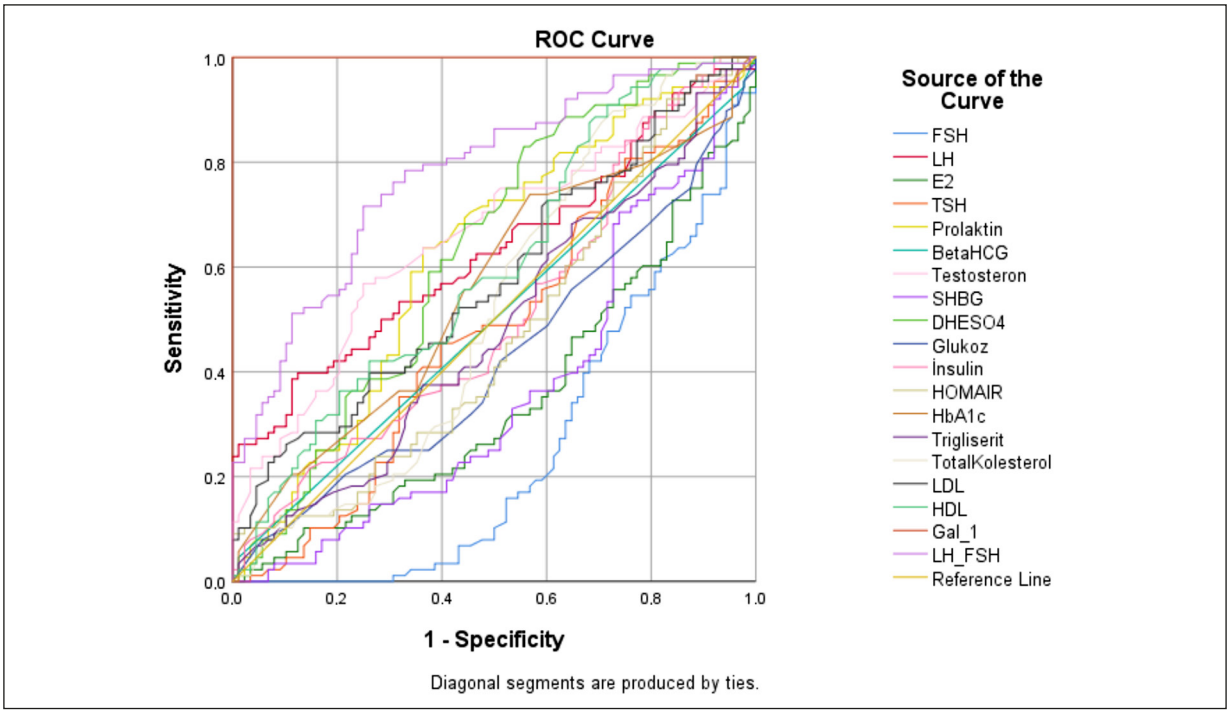

Figure 1. Determination of the cut-off point according to the ROC analysis.

Correlation Analysis between Gal-1 and Laboratory Markers of PCOS Patients

Gal-1 and DHESO4 showed a weak but statistically significant positive connection (p=0.05). (Table III, Figure 2).

Discussion

While PCOS increases the risk of developing gestational diabetes, preeclampsia, fetal macrosomia, small baby births and perinatal mortality in pregnant women, in the long term, it can lead to severe morbidities such as reproductive abnormalities, Type 2 diabetes, dyslipidemia, coronary heart disease, cancer, cerebrovascular morbidity, anxiety, and depression are just a few of the conditions that can cause insulin resistance[23].

In patients with PCOS, hypothalamus-pituitary-ovarian or adrenal axis abnormality and a relative increase in the release of FSH from LH have been found[24]. According to Saadia[25], women with PCOS's BMI, LH, FSH, LH/FSH ratios, and serum hormone levels do not significantly correlate with one another. Another study discovered a substantial difference between obese PCOS patients, non-obesity PCOS patients, and the control group in the FSH, LH, and E2 parameters[1]. In a retrospective study[26] conducted in 2020 with a number of large-scale patients, the LH/FSH ratio between PCOS and non-PCOS groups was determined as 1.27 and 0.61, respectively, in patients with BMI <25. In the same study, it was discovered that patients in the control group had much greater E2 levels than PCOS patients did[26]. No significant difference was discovered between PCOS and control patients' BMI or age characteristics in our investigation (p>0.05, Table I). PCOS and control group LH/FSH ratio was determined as 1.49 and 0.82, respectively. A statistically significant difference in FSH, LH, and E2 parameters between PCOS and control groups was found following the literature (p<0.05, Table II).

There are studies[27-29] on the prolactin levels of PCOS patients in the literature with varying conclusions. While Overgaard et al[27] reported no distinction in prolactin levels between the PCOS and control groups, some studies[28] have found a statistically significant difference between the groups. Prolactin and testosterone levels were observed to be noticeably higher in PCOS individuals with normal BMI compared to the control group by Franik et al[29]. In a different study[1],

Table IV. ROC Analysis Results of the blood values taken from the patients.

Test result variable(s)	Cuto9ff	Sensitivity	Specificity	AUC	*p*-value	Asymptotic 95% confidence interval	
						Lower Bound	Upper Bound
FSH	**6.3650**	**0.398**	**0.670**	**0.254**	**0.001***	**0.182**	**0.327**
LH	**5.7400**	**0.659**	**0.534**	**0.633**	**0.002***	**0.550**	**0.715**
E2	**43.9000**	**0.432**	**0.636**	**0.351**	**0.001***	**0.270**	**0.432**
TSH	1.4650	0.557	0.591	0.481	0.665	0.395	0.567
Prolactin	**13.2500**	**0.716**	**0.489**	**0.620**	**0.006***	**0.536**	**0.703**
BetaHCG	0.17800	0.943	0.977	0.500	0.996	0.414	0.585
Testosterone	**0.21150**	**0.739**	**0.500**	**0.659**	**0.001***	**0.578**	**0.740**
SHBG	**45.750**	**0.545**	**0.716**	**0.371**	**0.003***	**0.288**	**0.454**
DHESO4	**171.000**	**0.614**	**0.420**	**0.629**	**0.003***	**0.546**	**0.712**
Glucose	88.50	0.557	0.648	0.428	0.097	0.343	0.512
Insulin	7.1750	0.716	0.716	0.509	0.830	0.423	0.595
HOMAIR	1.7698	0.614	0.659	0.472	0.521	0.386	0.558
HbA1c	5.2550	0.739	0.580	0.558	0.187	0.472	0.643
Triglyceride	85.50	0.602	0.591	0.483	0.704	0.398	0.569
T. Cholesterol	139.50	0.716	0.625	0.522	0.614	0.435	0.609
LDL	85.650	0.739	0.636	0.577	0.077	0.493	0.662
HDL	45.500	0.727	0.602	0.602	0.019*	0.519	0.686
Gal-1	**8.97**	**0.997**	**0.716**	**0.997**	**0.001***	**0.687**	**0.917**
LH/FSH	**1.01**	**0.989**	**0.977**	**0.778**	**0.001***	**0.711**	**0.846**

*$p < 0.05$, AUC; area under the curve.

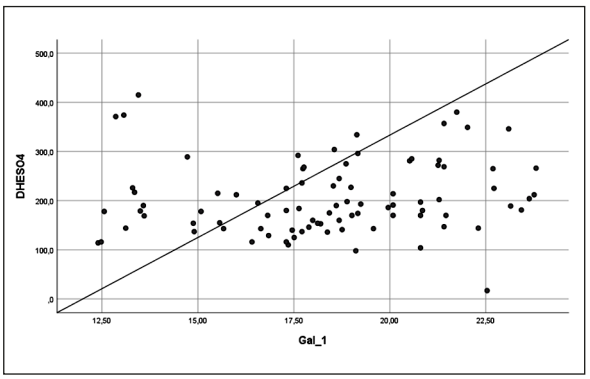

Figure 2. Correlation analysis of the relationship between Gal-1 and DHESO4.

the non-obese PCOS group's prolactin, testosterone, and DHEAS levels were considerably greater than those of the control group. In line with previous research[1,11], Our study demonstrated that the PCOS group's prolactin, testosterone, and dehydroepiandrosterone sulfate (DHEASO4) levels were substantially greater than those of the control group (p<0.05, Table II). The levels of testosterone and DHEAS in the PCOS group were found to be significantly higher than those in the control group in the study by Martinez-Garcia et al[30], while the levels of sex hormone binding protein (SHBG) were found to be significantly lower in the PCOS group than in the control group. In our investigation, the control group's SHBG values were statistically substantially higher than those of the PCOS patient group (p<0.05, Table II) than the PCOS patient group.

There is an increase in androgen synthesis in response to gonadotropins with increased ovarian sympathetic activity in PCOS patients, and there is a positive increase between this sympathetic activity and serum testosterone levels[31,32]. Inflammation mediates sympathetic dysfunction's effect on PCOS patients' hyperandrogenism[33]. In line with previous research[19], we discovered that PCOS patients had testosterone and dehydroepiandrosterone sulfate (DHEASO4) levels that were statistically substantially greater than those of the control group (p<0.05, Table II).

With an LH/FSH ratio of 0.778 AUC, a cut-off point of 1.01 was determined as a result of the ROC analysis, which corresponds to the point with the highest sensitivity and lowest specificity. In our study, the sensitivity of the LH/FSH ratio was 98.9%, and the specificity was 97.7% (95% CI 71.1-84.6%), while the sensitivity of testosterone was 73.9%, and the specificity was 50.0% (95% CI 57.8-74.0), which was found lower than the LH/FSH ratio (Table III, Figure 1). In our study, with an AUC value of 0.629, the sensitivity of the DHESO4 ratio was 61.4%, the specificity was 42.0% (95% CI 54.6-71.2%); the sensitivity and specificity of the prolactin level were 71.6% and 48.9% (95% CI 53.6-70.3%) (Table IV, Figure 1).

Galectins are involved in protein-protein interactions, cell growth, differentiation, survival, cell adhesion and modulation of cell migration in intracellular functions[34]. The Gal-1 expression has been reported in female and male reproductive organs[35,36]. There are changes in endometrial Gal-1 protein expression accompanying the regulation of steroid hormones during the menstrual cycle and pregnancy stages[35]. During immunological responses, cytokines from Th1- and Th2 effectors with pro- and anti-inflammatory properties control the homeostasis of endometrial tissue. Gal-1 participates in the control of the inflammatory immune response[37,38]. By enhancing CRH-mediated Gal-1 expression in macrophages, it has an immunomodulatory effect by promoting endometrial cell proliferation, remodeling, and angiogenesis. Gal-1, which is regulated by ovarian steroids, has an impact on blastocyst implantation and maternal-embryonic immune/endocrine-mediated placentation. Gal-1 expression alterations in the endometrium, trophoblastic tissue, menstrual cycle, and pregnancy have been observed in numerous investigations[39,40].

In our research, we discovered a statistically significant difference in Gal-1 levels between the PCOS and control groups (p=0.001, Table II). The cut-off point for the ROC analysis for Gal-1 was 8.97 points, which corresponded to the level of sensitivity and specificity with the highest and lowest values, respectively. At this level, the sensitivity of the scale was found to be 0.997 and the specificity was found to be 0.716 (95% CI: 68.7-91.7%). In addition, a statistically significant positive correlation was found between Gal-1 and DHESO4, an indicator of hyperandrogenism characterized by its increase in women with PCOS (p<0.05). The increase in Gal-1 levels due to the increase in DHESO4, a key marker of hyperandrogenism, which is one of the PCOS diagnostic criteria, once again demonstrated the value of Gal-1 protein as a clinical biomarker in polycystic ovary syndrome.

Conclusions

In this study, Gal-1 levels were investigated for the first time in PCOS patients. The high level of Gal-1 in PCOS patients whose etiopathogenesis is not fully explained suggests that it increases due to overexpression in response to inflammation. Gal-1 is also highly expressed and sensitive in PCOS-affected women, which suggests that this protein may be crucial in the etiology of the condition and will throw light on future studies.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

The study was started after obtaining the consent of Malatya Turgut Özal University Faculty of Medicine Interventional Clinical Research Ethics Committee (no: 2022/13). All procedures followed were in accordance with the Declaration of Helsinki.

Informed consent

All people included in the study were informed about it, and their consent was obtained.

Authors' Contribution

HA; Study concept and design, supervision, materials, data collection and/or processing, writing, analysis and/or interpretation. TRK; Statistical expertise, critical revision of the manuscript for important intellectual content. FI; analysis and interpretation of the data, administrative. EY; technical, or material support, study supervision.

References

1) Elci E, Kaya C, Cim N, Yildizhan R, Elci GG. Evaluation of cardiac risk marker levels in obese and non-obese patients with polycystic ovaries. Gynecol Endocrinol 2017; 33: 43-47.
2) Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil Steril 2016; 106: 6-15.
3) ACOG Practice Bulletin No. 108: Polycystic ovary syndrome. Obstet Gynecol 2009; 114: 936-949.
4) Legro RS, Arslanian SA, Ehrmann DA. Endocrine Society. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2013; 98: 4565-4592.
5) Trikudanathan S. Polycystic Ovarian Syndrome. Medical Clinics of North America 2015; 99: 221-235.
6) Duleba AJ, Dokras A. Is PCOS an inflammatory process? Fertil Steril 2012; 97: 7-12.
7) Shorakae S, Ranasinha S, Abell S, Lambert G, Lambert E, Courten B, Teede H. Inter-related effects of insulin resistance, hyperandrogenism, sympathetic dysfunction and chronic inflammation in PCOS. Clin Endocrinol 2018; 89: 628-633.
8) Velez LM, Seldin M, Motta AB. Inflammation and reproductive function in women with polycystic ovary syndrome†. Biol Reprod 2021; 104: 1205-1217.
9) Prapas Y, Petousis S, Panagiotidis Y, Gullo G, Kasapi L, Papadeothodorou A, Prapas N. Injection of embryo culture supernatant to the endometrial cavity does not affect outcomes in IVF/ICSI or oocyte donation cycles: a randomized clinical trial. Eur J Obstet Gynecol Reprod Biol 2012; 162: 169-173.
10) D'Anna R, Corrado F, Loddo S, Gullo G, Giunta L, Di Benedetto A. Myoinositol plus α-lactalbumin supplementation, insulin resistance and birth outcomes in women with gestational diabetes mellitus: a randomized, controlled study. Sci Rep 2021; 11: 8866.
11) Rotterdam ESHRE/ASRM-Sponsorerd PCOS Consensus Worksop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004; 81: 19-25.
12) Triguero-Martínez A, de la Fuente H, Montes N, Ortiz AM, Roy-Vallejo E, Castañeda S, González-Alvaro I, Lamana A. Validation of galectin-1 as potential diagnostic biomarker of early rheumatoid arthritis. Sci Rep 2020; 10: 17799.
13) Camby I, Le Mercier M, Lefranc F, Kiss R. Galectin-1: a small protein with major functions. Glycobiology 2006; 16: 137-157.
14) Elola MT, Chiesa ME, Alberti AF, Mordoh J, Fink NE. Galectin-1 receptors in different cell types. J Biomed Sci 2005; 12: 13-29.
15) Rabinovich GA, Rubinstein N, Toscano MA. Role of galectins in inflammatory and immunomodulatory processes. Biochim Biophys Acta 2002; 1572: 274-284.
16) Perillo NL, Pace KE, Seilhamer JJ, Baum LG. Apoptosis of T cells mediated by Galectin-1. Nature 1995; 378: 736-739.
17) Toscano MA, Bianco GA, Ilarregui JM, Croci DO, Correale J, Hernandez JD, Zwirner NW, Poirier F, Riley EM, Baum LG, Rabinovich GA. Differential glycosylation of TH1, TH2 and TH-17 effector cells selectively regulates susceptibility to cell death. Nat Immunol 2007; 8: 825-834.
18) Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab 1961; 21: 1440-1447.

19) Al Kindi MK, Al Essry FS, Al Essry FS, Mula-Abed W-AS. Validity of serum testosterone, free androgen index, and calculated free testosterone in women with suspected hyperandrogenism. Oman Med J 2012; 27: 471-474.

20) Otlu Ö, Erdem M, Korkmaz K, Ota Günay Ö, İn E, Kıran TR, Bay Karabulut A. Effect of Altered Iron Metabolism on Hyperinflammation and Coagulopathy in Patients with Critical COVID-19: A Retrospective Study. Int J Acad Med Pharm 2022; 4: 60-64.

21) Alpar R, Spor, Sağlık ve Eğitim Bilimlerinde Örneklerle Uygulamalı İstatistik ve Geçerlik-Güvenirlik, 6. Baskı, Detay Yayıncılık, Ankara 2020.

22) Dirican A. Tanı testi performanslarının değerlendirilmesi ve kıyaslanması. Cerrahpaşa Tıp Dergisi 2001; 32: 25-30.

23) Glintborg D, Andersen M. Morbidity in polycystic ovary syndrome. Eur J Endocrinol 2017; 176: R53-R65.

24) Yen SS. The polycystic ovary syndrome. Clin Endocrinol 1980; 12; 177-183.

25) Saadia Z. Follicle Stimulating Hormone (LH: FSH) Ratio in Polycystic Ovary Syndrome (PCOS) - Obese vs. Non-Obese Women Med Arch 2020; 74: 289-293.

26) Yang H, Di J, Pan J, Yu R, Teng Y, Cai Z, Deng X. The Association Between Prolactin and Metabolic Parameters in PCOS Women: A Retrospective Analysis. Front Endocrinol (Lausanne) 2020; 11: 263.

27) Overgaard M, Glintborg D, Christesen HT, Jensen TK, Andersen MS. Maternal prolactin is associated with glucose status and PCOS in pregnancy: Odense Child Cohort. Eur J Endocrinol 2020; 183: 307-316.

28) Kyritsi EM, Dimitriadis GK, Angelousi A, Mehta H, Shad A, Mytilinaiou M, Kaltsas G, Randeva HS. The value of prolactin in predicting prolactinoma inhyperprolactinaemic polycystic ovarian syndrome. Eur J Clin Invest 2018; 48: 12961.

29) Franik G, Madej P, Guz-Lem M, Owczarek A, Chudek J, Olszanecka-Glinianowicz M. Daytime decrease of prolactin levels is associated with PCOS regardless to nutritional status and other hormones levels. Gynecol Endocrinol 2017; 33: 336-341.

30) Martınez-Garcıa MA, Gambineri A, Alpanes M, Sanchon R, Pasquali R, Escobar-Morreale HF. Common variants in the sex hormone-binding globulin gene (SHBG) and polycystic ovary syndrome (PCOS) in Mediterranean women. Human Reproduction 2012; 27: 3569-3576.

31) Heider U, Pedal I, Spanel-Borowski K. Increase in nerve fibers and loss of mast cells in polycystic and postmenopausal ovaries. Fertil Steril 2001; 75: 1141-1147.

32) Barria A, Leyton V, Ojeda SR, Lara HE. Ovarian steroidal response to gonadotropins and beta-adrenergic stimulation is enhanced in polycystic ovary syndrome: role of sympathetic innervation. Endocrinology 1993; 133: 2696-2703.

33) Shorakae S, Ranasinha S, Abell S, Lambert G, Lambert E, Courten B, Teede H. Inter-related effects of insulin resistance, hyperandrogenism, sympathetic dysfunction and chronic inflammation in PCOS. Clin Endocrinol 2018; 89: 628-633.

34) Barrientos G, Freitag N, Tirado-Gonza´lez I, Unverdorben L, Jeschke U, Thijssen VLJL, Blois SM. Involvement of galectin-1 in reproduction: past, present and future. Hum Reprod Update 2014; 20: 175-193.

35) Choe YS, Shim C, Choi D, Lee CS, Lee KK, Kim K. Expression of galectin-1 mRNA in the mouse uterus is under the control of ovarian steroids during blastocyst implantation. Mol Reprod Dev 1997; 4: 261-266.

36) Özbek M, Hitit M, Yildirim N, Özgenç Ö, Ergün E, Ergün L. Expression pattern of galectin-1 and galectin-3 in rat testes and epididymis during postnatal development. Acta Histochem 2018; 120: 814-827.

37) Von Wolff M, Wang X, Gabius HJ, Strowitzki T. Galectin fingerprinting in human endometrium and decidua during the menstrual cycle and in early gestation. Mol Hum Reprod 2005; 11: 189-194.

38) Than NG, Erez O, Wildman DE, Tarca AL, Edwin SS, Abbas A. Severe preeclampsia is characterized by increased placental expression of galectin-1. J Matern Fetal Neonatal Med 2008; 21: 429-442.

39) Vergetaki A, Jeschke U, Vrekoussis T. Galectin-1 overexpression in endometriosis and its regulation by neuropeptides (CRH, UCN) indicating its important role in reproduction and inflammation. PLoS One 2014; 9: 1-17.

40) Vićovac L, Janković M, Cuperlović M. Galectin-1 and -3 in cells of the first trimester placental bed. Hum Reprod 1998; 13: 730-735.