PRACA ORYGINALNA/ORIGINAL PAPER

Endokrynologia Polska
DOI: 10.5603/EP.a2018.0002
Tom/Volume 69; Numer/Number 2/2018
ISSN 0423–104X

The impact of serum adropin and ischemia modified albumin levels based on BMI in PCOS

Stężenia adropiny i albuminy modyfikowanej niedokrwieniem w surowicy w zależności od występowania zespołu policystycznych jajników i wartości BMI

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Abstract

Introduction: The aim of this study was to evaluate the effects of polycystic ovary syndrome (PCOS) and body mass index (BMI) on serum adropin and ischemia modified albumin (IMA) levels.

Material and methods: This prospective cross-sectional study was performed with a total of 120 women [group1; non-PCOS = 60 (BMI < 25 = 30, BMI ≥ 25 = 30) and group 2; PCOS = 60 (BMI < 25 = 30, BMI ≥ 25 = 30)]. Blood samples were collected between the third and fifth days of the women's menstrual cycles after a night of fasting.

Results: There were no differences between the groups in relation to age, basal follicle stimulating hormone, estradiol, thyroid stimulating hormone, prolactin, high-density lipoprotein cholesterol, total testosterone, dehydroepiandrosterone sulfate levels, systolic and diastolic blood pressures. A significant difference was found in basal luteinizing hormone, fasting glucose, insulin, homeostatic model assessment of insulin resistance, total cholesterol, low-density lipoprotein cholesterol, triglycerides, free testosterone levels, waist-to-hip ratios and the Ferriman-Gallwey scores between the PCOS and non-PCOS patients in the lean and overweight groups ($P < 0.05$). The serum adropin levels in the lean PCOS group were lower than in the lean non-PCOS group ($P < 0.05$) and were lower in the overweight PCOS group than in the overweight non-PCOS group ($P < 0.05$). There was also a statistically significant difference in serum IMA levels in the PCOS group than in the non-PCOS group in both the lean and overweight groups ($P < 0.05$).

Conclusions: Although serum adropin levels were significantly decreased in the PCOS group, IMA levels increased. Further studies are needed to determine the effects of adropin and IMA in women with PCOS and to use a new marker to monitorize treatment outcomes. **(Endokrynol Pol 2018; 69 (2): 135–141)**

Key words: *adropin, ischemia modified albumin (IMA), insulin resistance, polycystic ovary syndrome (PCOS)*

Streszczenie

Wstęp: Badanie przeprowadzono w celu oceny wpływu zespołu policystycznych jajników (*polycystic ovary syndrome*, PCOS) i wskaźnika masy ciała (*body mass index*, BMI) na surowicze stężenia adropiny i albumin modyfikowanej niedokrwieniem (*ischemia modified albumin*, IMA).

Materiał i metody: To prospektywne badanie przekrojowe obejmowało 120 kobiet [grupa 1: osoby bez PCOS — n= 60 (BMI < 25 — n= 30; BMI ≥ 25 — n = 30) oraz grupa 2: osoby z PCOS — n= 60 (BMI < 25 — n= 30, BMI ≥ 25 —n = 30)]. Próbki krwi pobierano między trzecim a piątym dniem cyklu menstruacyjnego badanych kobiet, rano na czczo.

Wyniki: Grupy nie różniły się pod względem wieku, podstawowego stężenia hormonu folikulotropowego, stężeń estradiolu, tyreotropiny, prolaktyny, cholesterol frakcji HDL, testosteronu całkowitego i siarczanu dehydroepiandrosteronu ani skurczowego i rozkurczowego ciśnienia tętniczego. Stwierdzono natomiast istotne różnice między grupą z PCOS i bez PCOS w podgrupach osób szczupłych i otyłych w zakresie podstawowego stężenia hormonu luteinizującego, glikemii na czczo, wskaźnika insulinooporności w modelu homeostazy, stężeń cholesterolu całkowitego, cholesterolu frakcji LDL, triglicerydów i wolnego testosteronu, a także wskaźnika talia-biodra oraz oceny w skali Ferrimana-Gallweya ($P < 0,05$). Stężenia adropiny w osoczu były niższe w grupie szczupłych kobiet z PCOS niż u szczupłych osób niechorujących na PCOS ($P < 0,05$) oraz były niższe u otyłych osób z PCOS niż u otyłych osób z grupy bez PCOS ($P < 0,05$). Stwierdzono również statystycznie istotną różnice w stężeniach IMA w surowicy między kobietami z PCOS i bez PCOS, zarówno w podgrupie osób szczupłych, jak i otyłych ($P < 0,05$).

Wnioski: Mimo że surowicze stężenia adropiny były istotnie niższe w grupie z PCOS, stężenia IMA były podwyższone w tej grupie badanych. Konieczne są dalsze badania w celu określenia wpływu adropiny i IMA u kobiet z PCOS i stosowanie nowych wskaźników do monitorowania efektów leczenia. **(Endokrynol Pol 2018; 69 (2): 135–141)**

Słowa kluczowe: *adropina, albumina modyfikowana niedokrwieniem (IMA), insulinooporność, zespół policystycznych jajników (PCOS)*

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Introduction

Polycystic ovary syndrome (PCOS), which can cause hormonal, metabolic, and reproductive anomalies and is seen in 5–10% of women of reproductive age, is a chronic inflammatory endocrinopathy [1]. The etiology of PCOS, a complex heterogeneous disease thought to play a role in genetic and environmental factors, is not fully understood. Basic features of PCOS include ovulatory dysfunction, biochemical and clinical hyperandrogenism, and polycystic ovary appearance on ultrasonography (USG) [1, 2]. Defensive steroid biosynthesis and hyperinsulinemia associated with obesity-independent insulin resistance (IR) may increase the hyperandrogenism findings [2]. PCOS is associated with an increased risk of type 2 diabetes mellitus (DM) and cardiovascular disease due to atherosclerosis, metabolic syndrome, hyperlipidemia, hypertension, obesity, and oxidative stress. PCOS is also associated with infertility due to decreased oocyte maturation, fertilization, embryogenesis and miscarriage, preeclampsia, diabetes-related congenital abnormalities [3–6].

Adropin, which was discovered for the first time in 2008 by Kumar et al. [7], is a product of the energy homeostasis-associated (Enho) gene and a peptide-structured hormone containing 42 aminoacid, and is thought to play a role in the regulation of energy homeostasis and endothelial function [3, 7–10]. Lower adropin levels are associated with IR independent of obesity, dyslipidemia, hepatic steatosis, and increased fat mass. Overexpression or exogenous administration improves glucose homeostasis and increases blood flow and capillary density in rodents; it also has an endothelial protective role by increasing eNOS expression [7, 11]. Circulating adropin levels were found to be low in DM, gestational DM, metabolic syndrome, non-alcoholic fatty liver disease, PCOS, and coronary artery disease [5, 9, 10, 12, 13].

It has been reported that a change of N terminal structure of albumin occurs in cases of ischemic states in the human body, and a new molecule named ischemia-modified albumin (IMA), which cannot bind metal ions, is created [6, 14]. Higher IMA levels are observed more often in cases of myocardial ischemia, but can also increase in cases of type 2 DM, pulmonary embolism, liver cirrhosis, metabolic syndrome, and intrauterine pathologies [14, 15]. To our knowledge, serum IMA levels in patients with PCOS are in conflict with the literature. In addition to a study revealing that serum IMA levels did not change in patients with PCOS [16], other studies have shown that higher serum IMA levels are increasingly common [6, 17, 18].

In the current study, our aim was to investigate serum levels of adropin and IMA in women with PCOS.

Material and methods

A prospective sequential cross-sectional study was performed with a total of 120 women between January and December 2016 at the department of obstetric and gynecology, Konya Research and Education Hospital. Sixty PCOS patients and 60 age-and-BMI-matched non-PCOS patients with normal menstrual cycles were consecutively included. Clinical and demographic characteristics of all patients were evaluated by a single investigator. One hundred and twenty blood samples were analyzed. Patients were divided into subgroups according to BMI (BMI < 25 was considered lean and BMI ≥ 25 was considered overweight). This study was approved by the local ethics committee and the institutional review board.

Written and oral informed consent was obtained from all volunteers. The ethical principles for medical research involving human subjects stipulated in the 18th World Medical Association Declaration of Helsinki were applied. The BMI values and hormonal, biochemical, and ultrasonographic parameters were recorded. Sixty women (BMI < 25 = 30, BMI ≥ 25 = 30) were diagnosed with PCOS according to the menstrual, laboratory, and ultrasonographic criteria defined by a consensus workshop sponsored by ESHRE/ASRM in Rotterdam in May 2003 [19]. It includes: i = menstrual disorders oligoovulation/anovulation); ii = clinical and/or biochemical evidence of hyperandrogenism; and iii = polycystic ovaries on ultrasound examination (at least 10 follicles 2–9 mm in size or the volume of the ovary greater than 10 mL). Sixty non-PCOS women [(BMI < 25 = 30, BMI ≥ 25 = 30)] were evaluated as the control group. The Ferriman-Gallwey (FG) method was used to determine hirsutism [20]. Subjects were accepted as hirsute if their FG scores were ≥ 8. Biochemical hyperandrogenism was defined as an increase in the serum concentrations of free testosterone (normal values: 0.46–2.48 pg/dL) and/or total testosterone (normal values 0.15–0.7 ng/mL), according to manufacturer's instructions.

Control subjects were included from healthy women who visited the gynecology clinic for routine gynecological examination. The women in the control group had regular menstrual cycles (28–32 days) and no concomitant health problems or signs of hyperandrogenism.

The exclusion criteria were age < 18 or > 35 years, BMI ≥ 35 kg/m^2, evidence of clinical hyperandrogenemia (Cushing's syndrome, hyperprolactinemia, congenital adrenal hyperplasia, diseases of the adrenal gland,thyroid disorders, galactorrhea, breastfeeding, and pregnancy); type 1/type 2 diabetes; hypertension; active or chronic liver or renal failure, a history of coro-

nary artery disease; acute infection (within 14 days); the presence of any chronic inflammatory orautoimmune disease; known malignancy; hormonal contraception and/or anti-androgen therapy (within 6 months); and tobacco or alcohol use.

Study protocol

Anthropometric measurements including weight, height, and waist-to-hip ratio were peformed following detailed anamnesis and physical and gynecological examinations. Measurements of height and weight were performed with the subjects in light clothing. The BMI was calculated using the weight by the square of the height (weight/height^2–kg/m^2). Waist circumference (cm) was measured midway between the lower rib margin and the iliac crest at the level of the umbilicus during expiration. Hip circumference was calculated at the widest circumference at the level of the buttocks, and the waist-to-hip ratio (WHR) was calculated to assess body-fat distribution. Blood pressure was measured in the sitting position after a rest period of at least 5 minutes. IR was calculated using homeostatic model assessment of insulin resistance (HOMA-IR) and was calculated according to the following formula: fasting insulin (μIU/mL) x fasting glucose (mmol/L)/22.5) [21].

Biochemical evaluation

Venous blood samples were collected from the antecubital veins of all subjects from 8:00 a.m. and 10:00 a.m., between the third and fifth days of the menstrual cycle after a night of fasting. The plasma samples were stored at –80°C for adropin and IMA analysis. Thyroid stimulating hormone (TSH), prolactin, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E_2), fasting blood glucose (FBG), serum insulin, hs-CRP, total cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), free testosterone, total testosterone, dehydroepiandrosterone sulfate (DHEA-S), adropin, and IMA levels were measured on the day of sampling.

Serum FBG, hs-CRP, total cholesterol, HDL-C, LDL-C, and TG levels were measured by commercially available kits based on routine methods on the Olympus AU 5800 auto-analyzer (Beckman Coulter Inc., Fullerton, CA, USA).

Serum TSH, PRL, FSH, LH, testosterone, and E_2 levels were measured by Advia Centaw XP systems (Siemens Healthcare Diagnostics, Germany). Serum free testosterone was measured by Radio Immune Assay method (LB 2111 Multi Crystal Gamma Counter-Berthold, Germany).

Serum insulin and DHEA-S levels (NR:6-27mIU/mL) were measured by Immulite 2000 with the chemiluminescence immunometric method (Siemens Healthcare Diagnostics). The analytic sensitivity of the assay was 2 mlU/mL. Intra-assay variations as coeefficients of variation (CVs) for various insulin values were 5.5% (7.67 mlU/mL), 4.0% (12.5 mlU/mL), 3.3% (17.2 mlU/mL), 3.9% (26.4 mlU/mL), 3.8% (100 mlU/mL), and 3.7% (291 mlU/mL). Interassay variations for the insulin concentrations mentioned above were 7.3%, 4.9%, 4.1%, 5%, 4.2%, and 5.3%, respectively.

Serum adropin concentrations were measured by an enzyme-linked immunosorbent assay kit (Catalog No. 201-12-3107 Sunred Biological Technology Co., Shanghai, PRC) as recommended by the manufacturer's protocol. CVs for intra-assay were < 9%; CVs for inter assay were < 11%; sensitivity was 4,735 pg/mL; and assay range was 5–1000 pg/mL.

Serum IMA concentrations were measured by an enzyme-linked immunosorbent assay kit (Catalog No. 201-12-1173 Sunred Biological Technology Co., Shanghai, PRC) as recommended by the manufacturer's protocol. Sensitivity was 2,226 ng/mL; assay range was 3–600 ng/mL.

Statistical analysis

We used the SPSS 15 (Statistical Package for Social Sciences, SPSS Inc) software for statistical analyses. The distributions of all of the continuous variables for normal or abnormal distributions were tested using Shapiro-Wilk test. The homogenity of variances was evaluated using the Levene Test. Metric discrete and continuous variables are expressed as the mean ± SD, where applicable. Nominal data were expressed as the number of cases and percentages. Though the normal distributed variables between groups were compared using Student's *t* test, the Mann-Whitney *U* test was applied to the abnormal distributed variables. Nominal data were analyzed using Pearson's Chi square or Fisher's exact test, when appropriate. A p value < 0.05 was considered statistically significant. However, for all multiple comparisons, the Bonferroni adjustment was applied to control for Type I error.

Results

Table I describes demographic and clinical characteristics in patients based on PCO and BMI. No statistically significant differences were found between the groups in relation to age, basal FSH and estradiol, HDL-C, total testosterone, and DHEA-S, TSH, prolactin levels, systolic and diastolic blood pressures. There was a significant difference in basal LH, fasting glucose, insulin, HOMA-IR, total cholesterol, LDL-C, triglyceride, and free testosterone levels, waist-to-hip ratio and FG score between the PCOS and non-PCOS patients in the lean

Table I. *Demographic and clinical characteristics in patients based on PCO and BMI*

Tabela I. *Demograficzna i kliniczna charakterystyka chorych w zależności od występowania zespołu policystycznych jajników (polycystic ovary syndrome, PCOs) i wartości wskaźnika masy ciała (body mass index, BMI)*

Variables	Non-PCOS (n = 60)	PCOS (n = 60)	p-value[a]
Age [years]			
*BMI < 25 kg/m²	25.30 ± 5.59	25.91 ± 4.60	0.644
**BMI ≥ 25 kg/m²	26.97 ± 5.24	27.22 ± 4.52	0.845
p-value[b]	0.238	0.274	
TSH [μIU/mL]			
*BMI < 25 kg/m²	2.19 ± 1.20	1.72 ± 1.10	0.123
**BMI ≥ 25 kg/m²	1.83 ± 1.08	1.32 ± 0.95	0.057
p-value[b]	0.227	0.133	
Prolactin [ng/mL]			
*BMI < 25 kg/m²	11.32 ± 8.60	14.32 ± 7.47	0.155
**BMI ≥ 25 kg/m²	12.56 ± 6.81	15.50 ± 8.06	0.132
p-value[b]	0.539	0.559	
Basal FSH [IU/L]			
*BMI < 25 kg/m²	6.78 ± 1.65	7.24 ± 0.92	0.197
**BMI ≥ 25 kg/m²	6.85 ± 1.40	7.42 ± 1.19	0.096
p-value[b]	0.878	0.514	
Basal LH [IU/L]			
*BMI < 25 kg/m²	6.08 ± 1.86	10.61 ± 5.79	**< 0.001**
**BMI ≥ 25 kg/m²	6.28 ± 1.58	11.47 ± 6.57	**< 0.001**
p-value[b]	0.672	0.592	
Basal E_2 [pg/mL]			
*BMI < 25 kg/m²	56.04 ± 16.62	51.02 ± 11.70	0.181
**BMI ≥ 25 kg/m²	52.38 ± 6.43	49.37 ± 14.10	0.295
p-value[b]	0.268	0.626	
Waist to hip ratio			
*BMI < 25 kg/m²	0.74 ± 0.11	0.82 ± 0.09	**0.005**
**BMI ≥ 25 kg/m²	0.79 ± 0.10	0.92 ± 0.12	**< 0.001**
p-value[b]	0.125	**0.001**	
SBP [mmHg]			
*BMI < 25 kg/m²	105.00 ± 10.74	109.00 ± 9.94	0.140
**BMI ≥ 25 kg/m²	102.00 ± 10.30	106.67 ± 9.22	0.070
p-value[b]	0.274	0.351	
DBP [mmHg]			
*BMI < 25 kg/m²	66.00 ± 7.70	68.68 ± 5.07	0.119
**BMI ≥ 25 kg/m²	68.33 ± 8.33	71.17 ± 7.84	0.181
p-value[b]	0.265	0.149	
Ferriman-Gallwey score			
*BMI < 25 kg/m²	5.83 ± 1.05	15.90 ± 6.55	**< 0.001**
**BMI ≥ 25 kg/m²	6.361.58	16.63 ± 6.94	**< 0.001**
p-value[b]	0.131	0.676	
Fasting glucose			
*BMI < 25 kg/m²	75.10 ± 12.81	82.971 ± 1.63	**0.016**
**BMI ≥ 25 kg/m²	79.23 ± 6.01	84.17 ± 9.71	**0.021**
p-value[b]	0.115	0.611	
Insulin			
*BMI < 25 kg/m²	5.80 ± 5.04	12.68 ± 8.07	**< 0.001**
**BMI ≥ 25 kg/m²	6.87 ± 3.94	15.89 ± 13.37	**< 0.001**
p-value[b]	0.361	0.271	
HOMA-IR [mg/dL]			
*BMI < 25 kg/m²	1.11 ± 1.08	2.70 ± 1.89	**< 0.001**
**BMI ≥ 25 kg/m²	1.39 ± 0.72	3.43 ± 3.19	**0.002**
p-value[b]	0.361	0.271	
Insulin resistance [%]			
*BMI < 25 kg/m²	3 (10%)	12 (40%)	**0.015**
**BMI ≥ 25 kg/m²	9 (30%)	21 (70%)	**0.004**
p-value[b]	0.104	0.037	
LDL-C [mg/dL]			
*BMI < 25 kg/m²	109.03 ± 27.37	125.50 ± 27.06	**0.023**
**BMI > 25 kg/m²	114.70 ± 25.89	135.50 ± 35.10	**0.011**
p-value[b]	0.414	0.221	
HDL-C [mg/dL]			
*BMI < 25 kg/m²	51.57 ± 10.30	49.54 ± 10.22	0.455
**BMI > 25 kg/m²	47.77 ± 9.82	45.27 ± 9.28	0.434
p-value[b]	0.149	0.246	
Trigycerides [mg/dL]			
*BMI < 25 kg/m²	85.90 ± 20.93	126.27 ± 26.03	**< 0.001**
**BMI > 25 kg/m²	93.01 ± 26.89	136.17 ± 24.77	**< 0.001**
p-value[b]	0.259	0.137	
hs-CRP [mg/dL]			
*BMI < 25 kg/m²	1.86 ± 1.81	3.22 ± 2.78	**0.021**
**BMI > 25 kg/m²	2.11 ± 1.55	3.89 ± 2.90	**0.016**
p-value[b]	0.703	0.364	
Total testosterone [ng/mL]			
*BMI < 25 kg/m²	0.37 ± 0.13	0.41 ± 0.15	0.309
**BMI > 25 kg/m²	0.38 ± 0.12	0.43 ± 0.11	0.102
p-value[b]	0.813	0.551	
Free testosterone [pg/dL]			
*BMI < 25 kg/m²	1.15 ± 0.36	2.33 ± 0.56	**< 0.001**
**BMI > 25 kg/m²	1.35 ± 0.57	2.55 ± 0.62	**< 0.001**
p-value[b]	0.117	0.173	
DHEA-SO_4 [μg/dL]			
*BMI < 25 kg/m²	191.08 ± 97.98	228.88 ± 99.74	0.148
**BMI > 25 kg/m²	206.98 ± 69.88	245.63 ± 102.48	0.094
p-value[b]	0.472	0.527	

BMI — body mass index; TSH — thyroid stimulating hormone; FSH — follicle-stimulating hormone; LH —luteinizing hormone; E_2 — estradiol; HOMA-IR — homeostasis model assessment of insulin resistance; LDL-C — low density lipoprotein cholesterol; HDL-C — high density lipoprotein cholesterol; hs-CRP — high sensitivity C-reactive protein; DHEA-S — dehydroepiandrosterone sulfate; *BMI < 25kg/m² and Non-PCOS n = 30; BMI < 25kg/m² and PCOS n = 30

** BMI ≥ 25 kg/m² and Non-PCOS n = 30, BMI ≥ 25 kg/m² and PCOS n = 30; [a]: Comparisons of PCOS and non-PCOS groups. P < 0.025 set as statistically significant (Bonferroni adjustment was applied for controlling Type I error). [b]: Comparisons of BMI groups p < 0.025 set as statistically significant

and overweight groups ($P < 0.05$). Serum adropin and IMA levels, based on BMI and PCOS, are presented in Table II. We detected lower serum adropin levels in the lean PCOS group than in the lean non-PCOS group ($P < 0.05$) and in the overweight PCOS group than in the overweight non-PCOS group ($P < 0.05$). We also noted that there was a statistically significant difference in serum IMA levels in the PCOS group than in the non-PCOS group, in both the lean and overweight groups ($P < 0.05$).

Table II. *Adropin and IMA levels based on BMI and PCOS*

Tabela II. ***Stężenia adropiny i albuminy modyfikowanej niedokwieniem (ischemia modified albumin, IMA) w zależności od występowania zespołu policystycznych jajników (polycystic ovary syndrome, PCOS) i wartości wskaźnika masy ciała (body mass index, BMI)***

Variables	Non-PCOS	PCOS	p-value[a]
Adropin levels [ng/mL]			
*BMI < 25 kg/m²	479.47 ± 358.18	282.20 ± 85.22	**0.006**
**BMI ≥ 25 kg/m²	390.70 ± 259.25	254.67 ± 71.18	**0.009**
p-value[b]	0.276	0.180	
IMA levels [ng/mL]			
*BMI < 25 kg/m²	182.03 ± 105.76	294.47 ± 221.21	**0.016**
**BMI ≥ 25 kg/m²	224.93 ± 101.91	352.60 ± 228.31	**0.008**
p-value[b]	0.115	0.321	

BMI — body mass index; IMA — ischemia-modified albumin

*BMI < 25 kg/m² and Non-PCOS n = 30; BMI < 25 kg/m² and PCOS n = 30

** BMI ≥ 25 kg/m² and Non-PCOS n = 30, BMI ≥ 25 kg/m² and PCOS n = 30

[a]: Comparisons of PCOS and non-PCOS groups. $P < 0.025$ set as statistically significant (Bonferroni adjustment was applied for controlling Type I error). [b]: Comparisons of BMI groups $p < 0.025$ set as statistically significant

Discussion

In the present study, we sought to compare the impact of PCOS and BMI on serum adropin and IMA levels in patients with PCOS. In the PCOS group, although serum adropin levels were lower in lean and overweight patients with PCOS, serum IMA levels were higher than those in non-PCOS women.

The etiopathogenesis of PCOS is not fully known; some genetic and environmental conditions are responsible. It is estimated that IR plays the most important role in PCOS. In 70% of cases, PCOS can develop independently of obesity; this leads to an increase in androgen production, leading to menstrual disorders, polycystic ovary appearance, and hirsutism [2, 4, 13]. It is also suggested that IR causes glucose intolerance, type 2 DM, hypertension, dyslipidemia, and cardiovascular diseases [3–6, 22]. In addition, it is believed that visceral obesity, which is believed to be caused by IR, increases the incidence of DM and cardiovascular disease in patients with PCOS [5, 17]. Because of such conditions, PCOS is now regarded as a complex endocrinological disorder, not as a gynecological disease. While the IR should ideally be assessed using the clamp technique, the HOMA-IR method, which is less invasive, is preferred by clinicians. If the HOMA-IR value is above 2.5 mg/dL, IR is considered [21]. IR was found to be 64% in a study [23] involving 271 PCOS patients, 30% in lean PCOS cases, and 95% in obese PCOS cases in another study [13]. In our study, IR was found in 40% of the lean PCOS cases and 70% of the obese PCOS cases, compatible with the literature. It has been reported that oxidative stress, chronic inflammation, and ischemia may cause endothelial dysfunction and increase cardiovascular and metabolic complications in patients with PCOS [7, 11, 17].

In one study, WHR was shown to be increased in obese PCOS patients compared to lean PCOS patients and the control group [24]. In another study, no significant differences were found [17]. In our study, we observed that WHR increases in obese PCOS cases compared to lean PCOS cases and the control group, which is similar to the results in the first study.

There are many studies in the literature researching the relationship between PCOS and inflammatory markers, including hs-CRP. In addition to studies showing that hs-CRP increases in patients with PCOS [25, 26], studies show that this has not changed [17, 27, 28]. We also found that hs-CRP levels were higher in women with PCOS than in the control group. Higher hs-CRP levels in PCOS patients show that PCOS is a chronic inflammatory disease.

It has been shown that adropin, which is expressed in the central nervous system, liver, heart, and skeletal muscles, is thought to play a role in energy homeostasis; it has also been shown to reduce diets or genetically induced obesity in mice. Additionally, systemic administration or transgenic overexpression reduces IR and hepatosteatosis, and regulates glucose homeostasis [3, 7]. Adropin deficiency has led to increased fat mass and improved IR in mice [29]. In addition, adropin plays a role in glucose oxidation, activating pyruvate dehydrogenase and lipid oxidation inhibiting carnitine palmitoyl transferase [11]. Another study showed that intraperitoneal adropin administration in type 2 diabetic rats reduced fasting glucose levels, HOMA-IR, triglycerides, and HbA1c, and increased HDL levels [30]. From the aforementioned results, it can be concluded that adropin has a protective role against hepatosteatosis, hyperinsulinemia, and dyslipidemia. In addition, adropin has a protective effect on andothelial functions by increasing nitric-oxide release and activating eNOS [3]. Therefore, we think that adropin can be used as a potential biomarker to anticipate IR.

It has been shown that circulating adropin levels decreases in GDM, type 2 DM, metabolic syndrome, coronary artery disease, nonalcoholic fatty liver disease, and PCOS. Either adropin levels decreaseas a result of these disorders or lower adropin levels cause these diseases; this situation has not been fully clarified [5, 9, 10]. We also found in our study that, similar to the literature results [5, 9, 13], the circulating adropin levels in PCOS patients were statistically significantly lower than in the control group.

IMA, a marker of oxidative stress, is considered an indicator of ischemia and chronic hypoxia situation [6]. Chronic hypoxia and oxidative stress may play significant roles in PCOS due to IR [6, 17, 18]. IMA is a marker often studied in cardiac disorders and has been suggested to be a useful marker in cases of acute coronary syndrome and ischemic stroke [6, 15]. Several studies in the literature research serum IMA levels in patients with PCOS. Although some of them reported higher IMA levels [6, 10], others found no significant difference between PCOS patients and controls [16, 17]. In the present study, we found higher serum IMA levels in PCOS patients than in the control group. These higher IMA concentrations may be in accordance with higher triglyceride and low-density lipoprotein cholesterol levels.

The strengths of our study are that none of the cases in the PCOS and control groups included in the study had received any medical treatment that could affect the outcome of the study, and both groups were completely homegenous.

A potential weakness of our study is that we could not evaluate the visceral fat mass because the necessary method was costly, and the measurement technique was based on ionizing radiation. Another weakness of the current study was that HOMA-IR was used for IR instead of the gold standard method, the clamp technique.

In conclusion, we found that although circulating adropin levels decreased in women with PCOS, serum IMA levels were elevated at the end of our study. Future studies are warranted to clarify the effects of adropin and IMA in metabolic disorders such as PCOS. We believe that the results of our study will shed light on future work.

Compliance with ethical standards

Conflict of interest

The authors report no declarations of interest.

Ethical approval

This study was approved by the local ethics committee and the institutional review board.

Informed consent

Written informed consent was obtained from all volunteers.

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