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Investigation of relationship between nesfatin's, chemerin's, apelin's levels and insulin resistance and metabolic syndrome in Polycystic Ovary Syndrome patients

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Abstract

Polycystic ovary syndrome (PCOS) is one of the most common gynecological endocrinopathies. In the literature, many studies support the involvement of IR (insulin resistance) and some adipokines in the pathophysiology of PCOS. In our study, we aimed to investigate the relationships of apelin, chemerin, nesfatin, IR, and MS (metabolic syndrome) to help clarify the pathophysiology of PCOS. We included 120 people in our prospective cohort study. We divided these 120 cases into three equal groups: a control group of healthy participants and two case groups of participants suffering from PCOS with a BMI below 30 and above 30. We conducted this study in a tertiary hospital between January 2014 and July 2014. We investigated the study groups in terms of demographic information, biochemical values, hormonal parameters, apelin, chemerin, and nesfatin values, and the relationships between MS and IR. Apelin, chemerin, and nesfatin values were 0.233±0.027 ng/dl, 232.79±221.87 ng/dl, and 2.11±1.27 ng/dl in the control group. These values were 0.304±0.093 ng/dl, 313.57±379.04 ng/dl, and 0.85±0.91 ng/dl in the nonobese PCOS patient group, respectively. The same parameters were 0.304±0.093 ng/dl, 344.31±386.23 ng/dl, and 0.74±1.42 ng/dl in the obese PCOS patient group. The HOMA-IR values of the groups were 1.79 ± 0.68, 3.61 ± 5.45, and 4.58 ± 4.39, respectively. The distribution of cases diagnosed with MS within the groups was 0%, 10%, and 17.5%, respectively. We compared all these statistically significant results ($p<0.005$). The fact that blood nesfatin levels are significantly lower and apelin and chemerin levels are significantly higher in PCOS patients suggests that the synthesis and secretion of these adipokines are effective in the mechanism of the disease. The development of MS. Comprehensive prospective studies are needed to clarify this situation.

Keywords: apelin, chemerin, HOMA-IR, metabolic syndrome, nesfatin, PCOS

1. Introduction

Reliable publications report that although PCOS is quite common, it is seen in 5-10% of women of reproductive age and 3% of adolescents (1). For diagnosis, at least two Rotterdam criteria must be met, including oligo-anovulation, clinical or biochemical signs of hyperandrogenism, and ultrasonographic polycystic appearance in the ovaries (2). In the long term, patients suffering from PCOS are at increased risk for hypertension, infertility, recurrent spontaneous abortion, Type II DM (diabetes mellitus), dyslipidemia, coronary artery disease, endometrial hyperplasia, and cancer. Therefore, gynecologists and endocrinologists should investigate the physiopathology and the treatment of this syndrome with a multidisciplinary approach. However, the presence of many factors in the development of the syndrome and the heterogeneity in its presentation makes it difficult to understand its pathophysiology (3) fully.

Plasma apelin level increases significantly in obesity concerning hyperinsulinemia and insulin resistance (4). In this context, it might play a role in the pathophysiology of PCOS. Chemerin increases insulin resistance by preventing insulin-mediated glucose uptake in muscle cells (5). Chemerin is associated with central obesity, IR, hyperglycemia, dyslipidemia, HT, and prothrombotic and proinflammatory processes (6) It may play a role in the etiopathophysiology of PCOS due to its involvement in glucose uptake and being an adipokine. In line with the knowledge that nesfatin may be associated with glucose metabolism, insulin resistance and obesity development mechanisms (7, 8), it comes to mind that it may also be associated with the mechanism of PCOS formation. The etiopathogenesis of MS is multifactorial (9). It has been revealed that the basis of MS is a disorder in the response of tissues to insulin, that pancreatic β cells secrete

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more insulin than expected due to IR, and as a result, hyperinsulinemia develops (9). HT, dyslipidemia, obesity, DM, and atherosclerotic vascular disease are also components of MS due to IR and hyperinsulinemia (10). In line with all this information, we wondered how much MS and PCOS are related.

Although there are some hypotheses about the pathophysiology of PCOS when we review the literature, there still needs to be a clear consensus. We argue that some adipokines contribute to the formation of PCOS and that the discovery of the precise location of these molecules in human physiology may explain the mechanisms of PCOS formation. Regarding this subject, which needs all kinds of scientific studies to explain its pathophysiology, we aimed to explain the relationship between nesfatin, chemerin, apelin values, and MS and IR in PCOS patients.

2. Materials and methods

Our study was designed as a case-control study. It consists of 120 cases, including 80 patients aged 18-43 years and 40 healthy participants, diagnosed with PCOS according to the Rotterdam criteria. We conducted the study between January 2014 and July 2014 at Yüzüncü Yıl University, Faculty of Medicine, Department of Obstetrics and Gynecology. We informed the volunteers about the study before participating and obtained written consent from those who agreed to participate. Before the study, we received ethics committee approval from the Ethics Committee of the Yüzüncü Yıl university with the decision dated 30.01.2014 and numbered 05.

We recorded the patients' age, heights, and weights and calculated their body mass index (BMI). We evaluated the patients for hirsutism using the Ferriman-Gallwey scoring system. In the blood we collected on the third day of their menstrual cycles from all the cases participating in the study, we looked at luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), total testosterone, sex hormone binding globulin (SHBG), progesterone values. We measured low-density lipid (LDL), high-density lipid (HDL), triglyceride (TG), total cholesterol, fasting serum glucose, and insulin levels in the same blood samples of the subjects. We calculated the HOMA-IR index [Clear blood glucose (mg/dl) X fasting insulin level (µU/ml) / 405] using fasting blood glucose and fasting insulin levels. We also calculated the LH/FSH ratios. Our study used the MS diagnostic criteria of the Turkish Endocrinology Metabolism Society MS Study Group (11). We measured hormone parameters such as LH, FSH, E2, total testosterone, progesterone, SHBG, and fasting insulin using the immuno chemiluminescence method (Roche-Hitachi Modular Analytics E-170, USA). We measured fasting glucose, cholesterol, HDL, LDL, and TG from biochemical parameters by spectrophotometric method (Olympus AU 600 Tokyo / Japan). On the third day of menstruation, we collected 10 cc of blood from the antecubital vein between 08:00 and 10:00 in the morning, following a 10-hour night fast. We examined biochemical and hormonal parameters at Yüzüncü Yıl University, Faculty of Medicine, Department of Biochemistry. We rotated the separated 4 cc of the blood samples in a centrifuge at 5,000 rpm for 5 minutes, separated the serum into 2 cc epandorfs, and stored them at -80 0C until we checked the levels of Apelin, Chemerin, and Nesfatin in this serum. We measured Apelin, Chemerin, and Nesfatin levels using a micro-ELISA kit (Bio-Tek Instruments inc. Miroquant Cal / USA).

We used Siemens Acuson Antares™ USA brand device for ultrasonography of the patients. We used Siemens Acuson CH6-2 5.71 MHz abdominal probe USA for a suprapubic pelvic ultrasound and Siemens 47 Acuson EC9-4 6.15 MHz transvaginal probe USA for a transvaginal ultrasound.

2.1. Inclusion criteria

Participants between 18-43, diagnosed with PCOS, and whose BMI was determined were included in the case groups. For the control group, participants with regular menstrual cycles in the same age range and a BMI below 30 were included in the study.

2.2. Exclusion criteria

We excluded those suffering from diseases such as thyroid disease, prolactinoma, Cushing's disease, significant depression, DM (diabetes mellitus), HT (Hypertension), Dyslipidemia, CAD (coronary artery disease), late-onset adrenal hyperplasia, kidney and liver defect. In addition, we excluded those who use drugs that may affect sex hormone and carbohydrate metabolism.

2.3. Statistical analysis

We performed a One-Way Analysis of Variance (ANOVA) to compare group means in terms of continuous variables. We used Duncan's test to identify different groups following the analysis of variance. We separately calculated the Pearson correlation coefficients for the groups to determine the relationship between these variables.

We used SPSS for Windows 24.0 (SPSS Inc., Chicago, IL, USA) for the analyses. We presented the data as mean, standard deviation, and ratio and considered them statistically significant when the P value was less than 0.05.

3. Results

In our study, we found apelin values to be 0.233±0.027 ng/dl in the control group, 0.304±0.093 ng/dl in the nonobese PCOS patient group, and 0.311±0.042 ng/dl in the obese PCOS patient group. Apelin values were statistically significantly lower in the control group (p=0.0001). Chemerin levels, one of the main subjects of our study, were 232.79±221.87 ng/dl in the control group, 313.57±379.04 ng/dl in the nonobese PCOS patient group, and 344.31±386.23 ng/dl in the obese PCOS patient group. These differences between chemerin values were statistically significant (p=0.0001). Nesfatin values, another central theme of our study, were 2.11±1.27 ng/dl in the control group, 0.85±0.91 ng/dl in the nonobese PCOS patient

group, and 0.74±1.42 ng/dl in the obese PCOS patient group. These results were also statistically significant (p=0.0001). In our study, MS rates, one of the main lines of our research, were 0% in the control group, 10% in the nonobese PCOS patient group, and 17.5% in the obese PCOS patient group. This difference between the groups was statistically significant (p=0.001). We calculated the HOMA-IR values of the groups as 1.79±0.68 in the control group, 3.61±5.45 in the nonobese PCOS patient group, and 4.58±4.39 in the obese PCOS patient group, and the difference between these values was statistically significant (p=0.009) (Table 1).

Table 1. Demographic characteristics, hormonal and biochemical parameters in Control, Nonobese PCOS, and Obese PCOS patient groups

	Control n:40	Non-obese PCOS n:40	Obese PCOS n:40	P
Age (years)	27.5±7.84	24.63±5.04	26.75±5.35	0.104
BMI (kg/m^2)	23.33±2.62	22.4±2.51	31.74±2.06	0.001*
FGS	1.63±2.25	10.3±6.73	12±6.50	0.001*
Waist circumference (cm)	69.38±8.74	72.73±10.44	104.78±13.51	0.0001*
MS	0 (%0)	4 (%10)	7 (%17.5)	0.001*
FBG (mg/dl)	87.30±12	91.95±12.95	98.23±12.9	0.001*
Fasting insulin (mU/ml)	9.13±2.88	16.15±20.11	20.13±18.1	0.008*
Systolic BP (mmHg)	119±22	118±18	123±23	0.089
Diastolic BP (mmHg)	72±13	76±14	82±13	0.066
HOMA-IR	1.79±0.68	3.61±5.45	4.58±4.39	0.009*
HDL (mg/dl)	44.33±5.63	52.73±13.59	42.95±9.81	0.001*
LDL (mg/dl)	89.4±27.89	101.08±27.89	97.78±22.22	0.147
Cholesterol (mg/dl)	155.78±28.1	173.03±39.6	171.43±28.83	0.036*
Triglyceride (mg/dl)	96.85±38.02	96.25±53.54	143.15±113.21	0.008*
FSH (mIU/ml)	4.98±1.11	4.2±1.58	4.62±1.42	0.046*
LH (mIU/ml)	4.64±2.46	10.78±6.06	13.41±4.96	0.001*
Estradiol (pg/ml)	50.18±25.41	52.08±21.62	52.83±16.84	0.852
T. testosterone (ng/dl)	1.62±0.49	2.54±0.75	2.68±0.63	0.001*
SHBG (nmol/L)	99.17±30.99	39.51±39.1	24.82±10.52	0.001*
LH/FSH	0.94±0.55	2.67±1.21	3.11±1.33	0.001*
Nesfatin (ng/ml)	2.11±1.27	0.85±0.91	0.74±1.42	0.0001*
Chemerin (ng/ml)	232.79±221.87	313.57±379.04	344.31±386.23	0.0001*
Apelin (ng/ml)	0.233±0.027	0.304±0.093	0.311±0.042	0.0001*

One-way ANOVA *p<0.05, BMI: body mass index, FGS: Ferriman Galvey Score, HOMA-IR: Homeostatic Model Assessment insulin resistance, FBG: fasting blood glucose

We performed a Pearson correlation analysis between apelin, chemerin, and nesfatin values, metabolic syndrome, and insulin resistance in the obese PCOS patient group. We found a statistically significant negative correlation between apelin, chemerin, and nesfatin values and waist circumference (r=-0.398, p=0.006), (r=-0.282, p=0.039), (r=-0.368, p=0.01), (Table 2). there was also a statistically significant positive correlation between apelin, chemerin, and nesfatin values in the obese PCOS patient group (r=0.793, p<0.0001), (r=0.854, p<0.0001), (Table 2). Again, there was a statistically significant positive correlation between the chemerin and nesfatin values of the same group (r=0.596, p<0.0001) (Table 2).

Table 2. Correlation table between apelin, nesfatin, chemerin, IR, and MS criteria in the obese PCOS patient group

		Glucose	Insulin	HOMA -IR	Systolic BP	Diastolic BP	TG	HDL	BMI	WC	Apelin	Chemerin	Nesfatin
Apelin	r	-0.092	-0.050	-0.058	-0.088	-0.088	-0.155	0.016	-0.185	-0.398**	1	0.793**	0.854**
	p	0.285	0.380	0.361	0.295	0.294	0.169	0.460	0.126	0.006		0.0001	0.0001
Chemerin	r	-0.074	-0.059	-0.065	-0.082	-0.083	-0.164	0.088	-0.226	-0.282*	0.793**	1	0.596**
	p	0.325	0.359	0.344	0.308	0.306	0.156	0.295	0.080	0.039	0.0001		0.0001
Nesfatin	r	-0.105	-0.172	-0.182	-0.050	-0.050	-0.169	0.004	-0.236	-0.368**	0.854**	0.596**	1
	p	0.259	0.144	0.131	0.381	0.380	0.148	0.491	0.071	0.010	0.0001	0.0001	

WC: Waist Circumference; Pearson correlation test, **<0,01, *<0,05

There was a statistically significant negative correlation between apelin, chemerin, and nesfatin values and waist circumference in the nonobese PCOS patient group (r=-0.321, p=0.022), (r=-0.417, p=0.004), (r=-0.329, p=0.019), (Table 3). We found a positive correlation between apelin, chemerin, and nesfatin values in this group. This correlation was statistically significant (r=0.655, p<0.0001), (r=0.610, p<0.0001), (Table 3). Again, a statistically significant positive correlation was observed between chemerin and nesfatin values in the same group (r=0.546, p<0.0001) (Table 3).

Table 3. Correlation table between apelin, nesfatin, chemerin, IR, and MS criteria in the non-obese PCOS patient group

		Glucose	Insulin	HOMA -IR	Systolic BP	Diastolic BP	TG	HDL	BMI	WC	Apelin	Chemerin	Nesfatin
Apelin	r	0.035	0.009	0.015	0.000	-0.003	-0.131	-0.057	-0.187	-0.321*	1	0.655**	0.610**
	p	0.416	0.477	0.464	0.500	0.493	0.209	0.364	0.124	0.022		0.0001	0.000
Chemerin	r	0.163	-0.011	-0.011	-0.003	-0.008	-0.119	-0.204	-0.156	-0.417**	0.655**	1	0.546**
	p	0.158	0.474	0.474	0.492	0.480	0.233	0.103	0.169	0.004	0.0001		0.0001
Nesfatin	r	-0.001	0.094	0.068	0.005	-0.007	-0.034	0.008	-0.236	-0.329*	0.610**	0.546**	1
	p	0.499	0.283	0.339	0.489	0.482	0.418	0.481	0.071	0.019	0.0001	0.0001	

WC: Waist Circumference; Pearson correlation test, **<0,01, *<0,05

Our study found a statistically significant positive correlation between apelin values and diastolic blood pressure in the control group (r=0.329, p=0.019) (Table 4). In the same group, we found a negative correlation between chemerin values and TG values and a positive correlation between nesfatin values (r=-0.270, p=0.046) (r=0.864, p<0.0001) (Table 4). Again, this group had a positive correlation between nesfatin values and fasting blood glucose values. This correlation was statistically significant (r=0.265, p=0.049) (Table 4).

Table 4. Correlation table between apelin, nesfatin, chemerin, IR, and MS criteria in the control group

		Glucose	Insulin	HOMA -IR	Systolic BP	Diastolic BP	TG	HDL	BMI	WC	Apelin	Chemerin	Nesfatin
Apelin	r	0.071	-0.037	0.019	-0.007	0.329*	0.029	0.017	-0.130	-0.182	1	0.004	0.200
	p	0.333	0.410	0.454	0.482	0.019	0.428	0.459	0.212	0.131		0.491	0.108
Chemerin	r	0.229	-0.078	0.018	-0.205	0.032	-0.270*	0.197	-0.152	-0.046	0.004	1	0.864**
	p	0.078	0.316	0.456	0.102	0.421	0.046	0.112	0.175	0.390	0.491		0.0001
Nesfatin	r	0.265*	-0.048	0.055	-0.254	0.049	-0.134	0.196	-0.110	-0.076	0.200	0.864**	1
	p	0.049	0.384	0.367	0.057	0.381	0.205	0.112	0.250	0.320	0.108	0.0001	

WC: Waist Circumference; Pearson correlation test, **<0,01, *<0,05

According to the design of our study, there was a statistically significant difference between the groups' BMI, FGS, waist circumference, LH/FSH ratio, SHBG, total testosterone, LH, FSH, fasting insulin, TG, cholesterol, HDL, FBG values (p<0.05).

4. Discussion

Approximately 10-30% of PCOS patients have overt IR (12). Consistent with the literature, we found that IR was high in subjects suffering from PCOS, regardless of BMI. There is impaired glucose tolerance at a rate of 30-35% in PCOS patients (13). In our study, fasting blood glucose values were high in PCOS patient groups, which supports the literature. Also, insulin levels were higher in PCOS patient groups (12, 13).

It has been shown that the plasma concentration of apelin is two times higher in overweight individuals and five times higher in morbidly obese compared to nonobese individuals (14, 15). In our study, we found apelin values higher in patient groups which is parallel with the literature.

When we searched the literature, it was understood that there were inconsistencies between the apelin levels of the control and patient groups. In a study by Altınkaya et al., apelin levels were lower in PCOS patients compared to the control group, unlike our study (16). In some studies, no statistical difference was found between the apelin values among the groups (17). Studies on more extensive series are needed to clarify this situation. There was a statistically significant positive correlation between apelin values and diastolic blood pressure, one of the MS components. As far as we understood from the literature, we attributed this situation to the positive inotropic effect of apelin (18). Apelin values were negatively correlated with waist circumference in obese and nonobese PCOS patients. This situation contradicts the existing information in the literature when we consider the relationship between apelin and obesity. We attributed this to the limited number of cases in our study.

In conclusion, plasma apelin levels were higher in PCOS patients than in the healthy control group in our study. When we evaluate this situation in a cause-effect relationship, it may be caused by obesity, increased adiposity, changes in adipocytokine levels, impaired LH/FSH interaction, IR, hypothalamic-pituitary axis effects, or local paracrine and endocrine behaviors. Depending on the metabolic changes that occur in PCOS, it can also develop with a compensatory mechanism. Further studies are needed to elucidate this mechanism.

Contrary to our study, in some studies, nesfatin values were higher in-patient groups (19, 20). We think that this difference between various studies may be caused by different variables such as the ethnic structures, diets, and lifestyles of the study groups. This problem can be solved by conducting comprehensive studies. One study found a positive correlation between nesfatin and BMI and HOMA-IR (19). Another study conducted in the same year found a negative correlation between BMI, fasting blood sugar, insulin, HOMA-IR, and nesfatin (20). While a positive correlation was observed between nesfatin and HOMA-IR in one publication, a negative correlation was observed in another (19, 21). We found a negative correlation between nesfatin values and waist circumferences in obese and nonobese patient groups. However, no study in the literature shows a clear relationship

between waist circumference and nesfatin values. Deniz et al. found a negative correlation between BMI values and nesfatin levels (20). Based on this information, this finding is indirectly supported by the literature. Although we found a positive correlation between nesfatin and fasting blood sugar in the control group, Deniz et al. found a negative correlation between FBG and nesfatin levels (20). However, while they discovered this negative correlation in the patient group, we found a positive correlation in our study in the healthy control group. Although we encountered a similar situation when we examined the literature, this can be explained by the increase in nesfatin values, which have an antihyperglycemic effect in healthy individuals to lower blood sugar. In a study conducted by Hiroyuki S. et al., it was reported that subcutaneous nesfatin replacement could be used to treat obesity in the future (22). Considering that nearly half of PCOS patients are obese, it comes to mind that obesity and even PCOS can be prevented with possible nesfatin replacement therapy in the future. Therefore, it can be used as a new treatment method that reduces IR. It is conceivable that both ligand and receptor components of the nesfatin signaling system can be found in ovarian tissue and that this new molecule may have potential regulatory roles in physiological and pathological conditions in the ovary. The decrease in nesfatin levels in women with PCOS may play a role in developing PCOS via the hypothalamo-pituitary-gonadal axis. In order to explain this situation more clearly, studies with extensive cases are needed.

It has been reported that the blood concentration of chemerin is high in obese individuals. It has been reported that BMI, TG level and blood pressure are associated with chemerin levels, and chemerin affects the pathogenesis of DM and MS complications (23). Chemerin values detected in our study were statistically significantly higher in PCOS patient groups, similar to those of Ademoğlu et al., conducted in 2014 (24). Chemerin values were negatively correlated with TG values of the control group, while they were negatively correlated with waist circumferences of the obese and nonobese PCOS patient groups. When we searched the literature, we could not find any information about waist circumferences, while TG and chemerin were positively correlated in some studies in PCOS patient groups (24). However, since a positive correlation was found with BMI in the publications we reviewed, we think there may be an indirect positive correlation with waist circumference. The negative correlation of TG and chemerin values in healthy individuals in our study supports the literature indirectly. We found a positive correlation between chemerin and nesfatin values in the control group. We could not find any information about this correlation in the literature. The working principles of both adipokines can explain this situation. In addition, when we reviewed the literature extensively, we tried to find a study investigating the relationship between nesfatin, chemerin, and apelin in patients with PCOS. This study found a statistically significant positive correlation between nesfatin, apelin, and chemerin in the obese PCOS patient group. We hope to inspire new studies to be planned in the future and shed light on the pathophysiology of PCOS.

Blood lipid levels in women with PCOS differ from women with regular menstrual cycles. The first researchers to investigate this situation were Wild et al. (25). MS is a fatal endocrinopathy that begins with IR and combines with abdominal obesity, glucose intolerance, or systemic disorders such as DM, dyslipidemia, HT, and coronary artery disease. It has been suggested that MS patients have an increased risk of cardiovascular disease and diabetes, as well as an increased risk of PCOS, non-alcoholic fatty liver disease, gallstones, asthma, sleep disorders, and some types of cancer (26). All over the world, the nutritional habits and sedentary lifestyles brought about by modern urban life have increased the prevalence of obesity and diabetes. Parallel to this situation, an increase in obesity and DM, a significant increase was observed in the number of patients with MS (27). HOMA-IR, fasting insulin, fasting blood glucose, HDL, total cholesterol, and TG values were statistically significantly higher in the patient groups compared to all groups. The number of MS cases in the patient groups was naturally higher in the obese PCOS group. We did not find a case in the control group that met the diagnostic criteria for MS. These results support the information in the literature and show that the number of MS increases in PCOS patients (27).

In line with all this information, it is understood that PCOS patients also face a problem, such as MS, that increases mortality and morbidity. In the long run, PCOS increases the likelihood of exposure to many chronic diseases. In this context, to reduce the morbidity and mortality of patients, people suffering from PCOS should pay attention to their diet and stay away from a sedentary life. Most importantly, the etiopathophysiology of PCOS should be understood as soon as possible, and appropriate treatments should be discovered in this way.

The low levels of nesfatin in the patient groups in our study bring to mind the idea that nesfatin can be used as a drug in obesity and PCOS patients. High levels of chemerin and apelin in patient groups suggest that they play a role in the pathophysiology of insulin resistance and PCOS. We think that they cause MS's development, especially in PCOS cases. More comprehensive studies are needed to elucidate all these relationships. We found that the frequency of metabolic syndrome increased in obesity and PCOS. This situation shows us that PCOS and obesity can indirectly progress to mortality and morbidity. Initiating treatment as soon as the syndrome is detected in cases with PCOS will reduce the mortality and morbidity of women in this group due to these chronic diseases. In this context, PCOS patients should be treated conservatively, medically, and additionally with close follow-up periods.

Ethical Statement

The volunteers were informed about the study before participating, and written consent was obtained from those who agreed to take part. Ethical approval from the Ethics Committee of Yüzüncü Yıl University was received before the study, with the decision dated 30.01.2014 and numbered 05.

Conflict of interest

The authors reported no potential conflict of interest.

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Nothing to declare.

Authors' contributions

Concept: O.U., Z.K., Design: O.U., O.K., Z.K., Data Collection or Processing: O.U., O.K., Z.K., Analysis or Interpretation: O.U., O.K., Z.K., Literature Search: O.K., Z.K., Writing: O.K. Z.K.

References

1. Hashemipour M, Faghihimani S, Zolfaghary B, Hovsepian S, Ahmadi F, Haghighi S. Prevalence of polycystic ovary syndrome in girls aged 14-18 years in Isfahan, Iran. Horm Res 2004;62:278-282.
2. 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 Jan;81(1):19-25.
3. Speroff L. Anovulation and Polycystic ovary. Speroff L Fritz M.A. (editors). Clinical Gynecologic Endocrinology and Infertility. 6th ed. Philadelphia Pa, Lippincott Williams & Wilkins. 2005:465-491.
4. Bełtowski J. Apelin and visfatin: unique "beneficial" adipokines upregulated in obesity? Med Sci Monit. 2006;12:112-119.
5. Sell H, Laurencikiene J, Taube A, Eckardt K, Cramer A, Horrighs A, et al. Chemerin is a novel adipocyte-derived factor inducing insulin resistance in primary human skeletal muscle cells. Diabetes. 2009 Dec;58(12):2731-40.
6. Kershaw EE, Flier JS. Adipose tissue is an endocrine organ. J Clin Endocrinol Metab. 2004;89:2548–56.
7. Riva M, Nitert MD, Voss U, Sathanoori R, Lindqvist A, Ling C, et al. Nesfatin-1 stimulates glucagon and insulin secretion and beta cell NUCB2 is reduced in human type 2 diabetic subjects. Cell Tissue Res. 2011 Dec;346(3):393-405.
8. Gonzalez R, Perry RL, Gao X, Gaidhu MP, Tsushima RG, Ceddia RB, et al. Nutrient responsive nesfatin-1 regulates energy balance and induces glucose-stimulated insulin secretion in rats. Endocrinology. 2011;152:3628-37.
9. Isıldak M, Sain Güven G, Gürlek A. Metabolik sendrom ve insulin direnci Hacettepe Tıp Dergisi 2004;35:96-9.
10. Endokrinoloji Metabolizma ve Diabet. Özata M, Yönem A. (Editörler). 1. baskı. İstanbul Medical Yayıncılık; 2006: 550-63.
11. METABOLİK SENDROM KILAVUZU © Türkiye Endokrinoloji ve Metabolizma Derneği • 2009
12. Avi Ben-Haroush, Yariv Y, Benjamin F. Insulin resistance and metformin in polycystic ovary syndrome. Eur J of Obstet Gynecol and Reprod Biology 2004;115:125-33.
13. Cibula D, Cifkova R, Fanta M, Polende R, Zivny J, Skibova J. Increased risk of NIDDM, arterial hypertension and coronary artery disease in perimenopausal women with a history of the polycystic ovary syndrome. Hum Reprod 2000;15:785-789.
14. Boucher J, Masri B, Daviaud D, Gesta S, Guigné C, Mazzucotelli A, et al. Apelin, a newly identified adipokine up-regulated by insulin and obesity. Endocrinology, 2005;146:1764–71.
15. Heinonen MV, Purhonen AK, Miettinen P, Pääkkönen M, Pirinen E, Alhava E, et al. Apelin, orexin-A and leptin plasma levels in morbid obesity and effect of gastric banding. Regul Pept. 2005 Aug 15;130(1-2):7-13.
16. Altinkaya SÖ, Nergiz S, Küçük M, Yüksel H. Apelin levels in relation with hormonal and metabolic profile in patients with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol. 2014 May;176:168-72.
17. Benk Silfeler D, Gokce C, Keskin Kurt R, Yilmaz Atilgan N, Ozturk OH, Turhan E, et al. Does polycystic ovary syndrome itself have additional effect on apelin levels? Obstet Gynecol Int. 2014;2014:536896.
18. Lee DK, George SR, O'Dowd BF. Unraveling the roles of the apelin system: prospective therapeutic applications in heart failure and obesity. Trends Pharmacol Sci 2006;27:190-194.
19. Ademoglu EN, Gorar S, Carlıoglu A, Yazıcı H, Dellal FD, Berberoglu Z, et al. Plasma nesfatin-1 levels are increased in patients with polycystic ovary syndrome. J Endocrinol Invest. 2014 Aug;37(8):715-9.
20. Deniz R, Gurates B, Aydin S, Celik H, Sahin I, Baykus Y, et al. Nesfatin-1 and other hormone alterations in polycystic ovary syndrome. Endocrine. 2012;42:694-9.
21. Hamburg R. Management of polycystic ovary syndrome in adolescence. Reviews in Gynecological Practice 2004;4:148-155.
22. Shimizu H, Oh-I S, Okada S, Mori M. Nesfatin-1: an overview and future clinical application. Endocr J. 2009;56:537-543.
23. Bozaoglu K, Bolton K, McMillan J, Zimmet P, Jowett J, Collier G, et al. Chemerin is a novel adipokine associated with obesity and metabolic syndrome. Endocrinology. 2007 Oct;148(10):4687-94.
24. Ademoglu E, Berberoglu Z, Carlioglu A, Dellal F, Gorar S, Alphan Z, et al. Higher levels of circulating chemerin in both lean and obese patients with polycystic ovary syndrome. Minerva Ginecol. 2014 Dec;66:535-42.
25. Wild RA. Obesity, lipids, cardiovascular risk, and androgen excess. Am J Med 1995;98:27-32.
26. Legro RS. Polycystic ovary syndrome and cardiovascular disease: a premature association? Endocr Rev. 2003;24:302-12.
27. Creatsa M, Armeni E, Stamatelopoulos K, Rizos D, Georgiopoulos G, Kazani M, et al. Circulating androgen levels are associated with subclinical atherosclerosis and arterial stiffness in healthy recently menopausal women. Metabolism. 2012;61:193-201.