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Research Article

Estimation of Fibulin-1, Chemerin and Omentin-1 in Iraqi Women with Polycystic Ovary Syndrome-Associated Infertility

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Abstract

Background: Adipokines (fibulin-1, chemerin, and omentin-1) affect the hypothalamic-pituitary-gonadal axis and ovarian steroidogenesis. Adipocyte-secreted adipokines are dysregulated in females with polycystic ovarian syndrome (PCOS). ***Objective***: To investigate the role of serum fibulin-1, chemerin, omentin-1, total cholesterol (TC), high-density lipoprotein (HDL), triglyceride (TG), progesterone (PROG), and prolactin (PRL) in PCOS and the development of infertility. ***Methods***: 150 PCOS, infertile PCOS women and control women aged 20–40 years were enrolled in this observational study and divided into three groups: 40 women who were control, 60 women who had PCOS only and 50 women who had infertility and PCOS. Analyses of fibulin-1, chemerin, omentin-1, lipid profile, PROG, and PRL were performed for all participants. ***Results***: The results showed elevated levels of fibulin-1, chemerin, and PRL in both PCOS and infertile PCOS when compared with control, while omentine-1 and PROG decreased in both PCOS and infertile PCOS when compared with control. The levels of TC, HDL, and TG weren't affected in PCOS alone, but in cases of infertility, TC and TG increased while HDL decreased. ***Conclusions***: The increased level of fibulin-1 may be a new marker for PCOS and infertility. Chemerin shows a high level in both infertile PCOS and PCOS women, while omentin-1 shows a low level in both infertile PCOS and PCOS women.

Keywords: Chemerin, Fibulin-1, Infertility, Omentin-1, Polycystic ovary syndrome.

قياس مستويات فيبولين-1 وكيمرين و أومنتين-1 لدى النساء العراقيات المصابات بالعقم المرتبط بمتلازمة المبيض المتعدد الأكياس

الخلاصة

الخلفية: تؤثر الأديبوكينات (فيبولين -1، كيمرين، و أومنتين -1) على محور الغدة النخامية والغدد التناسلية وتكوين الستيرويد المبيض. الأديبوكينات التي تفرزها الخلايا الشحمية غير منظمة في الإناث المصابات بمتلازمة المبيض المتعدد الكيسات. **الهدف**: التحقيق في دور فيبولين المصل -1، والكيميرين ، و أومنتين-1، والكوليسترول الكلي، والبروتين الدهني عالي الكثافة، والدهون الثلاثية، والبروجسترون، والبرولاكتين في متلازمة تكيس المبايض وتطور العقم. **الطريقة**: تم تسجيل 150 من مريضات متلازمة تكيس المبايض ونساء متلازمة تكيس المبايض والعقم والنساء الطبيعيات اللائي تتراوح أعمارهن بين 20 و 40 عاما في هذه الدراسة القائمة على الملاحظة وقسمن إلى ثلاث مجموعات: 40 امرأة تم التحكم فيها، و 60 امرأة مصابة بمتلازمة تكيس المبايض فقط و 50 امرأة مصابة بالعقم ومتلازمة تكيس المبايض. تم إجراء تحليلات للفيبولين -1 ، والكيميرين ، و أومنتين-1، وصورة الدهون ، والبروجستيرون، والبرولاكتين لجميع المشاركين. **النتائج**: أظهرت النتائج مستويات مرتفعة من فيبولين-1 وكيميرين وبرولاكتين في كل من حالات متلازمة تكيس المبايض ومتلازمة تكيس المبايض مع العقم عند مقارنتها بالمجموعة الضابطة، بينما انخفض أومنتين-1 والبروجستيرون في كل من متلازمة تكيس المبايض ومتلازمة تكيس المبايض مع العقم عند مقارنتها بمجموعة السيطرة. لم تتأثر مستويات TC و HDL و TG في متلازمة تكيس المبايض وحدها، ولكن في حالات العقم، زاد TC و TG بينما انخفض HDL-c. **الاستنتاجات**: زيادة مستوى فيبولين-1 قد يكون علامة جديدة لمتلازمة تكيس المبايض والعقم. يظهر الكيميرين مستوى مرتفعا في كل من مريضات متلازمة تكيس المبايض العقيمة ومتلازمة تكيس المبايض، بينما يظهر أومنتين-1 مستوى منخفضا في كل من متلازمة تكيس المبايض العقيمة ومتلازمة تكيس المبايض لدى النساء.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is characterized by the presence of both clinical manifestations and physiological abnormalities related to excessive testosterone levels and impaired ovarian function, without any concurrent diagnostic diagnosis [1,2]. Polycystic ovarian syndrome (PCOS) is a complex endocrine disorder characterized by a combination of many clinical features, including menstrual irregularities, increased testosterone levels, and the presence of cystic ovaries [3,4]. The condition, known as Stein Leventhal syndrome, is acknowledged in honor of the two physicians who initially found it in 1935 [5]. Based on the criteria established by the National Institutes of Health (NIH), the present worldwide incidence of PCOS stands at 6% (with a range of 5% to 8%). However, when employing the Rotterdam or the androgen excess and PCOS society (AE-PCOS Society) criteria, the prevalence increases to 10% [6]. Polycystic ovary syndrome is a prevalent endocrine illness observed in women of reproductive age, with a prevalence rate ranging from 5% to 10% within the fertile female population. Among those affected, around 4% to 8% are young adults and middle-aged women. The observed outcomes can be attributed to significant epigenetic and environmental factors, as well as modifications in lifestyles, stress levels, and dietary patterns [1]. Moreover, there is a growing prevalence of this phenomenon among adolescent females, typically emerging shortly after the onset of puberty. Adipokines are chemicals that have been found to affect the hypothalamic-pituitary-gonadal axis and can also change the production of steroids in the ovaries. The dysregulation of adipocyte-secreted adipokines has been documented in women diagnosed with PCOS. Fibulin-1, a protein present in the extracellular matrix, is becoming acknowledged as a substantial factor in the development of endothelial disorders, including PCOS. Moreover, it serves pivotal roles in the mechanism of wound healing and has been associated with numerous respiratory disorders [7]. Fibulin-1 belongs to a group consisting of eight glycoproteins found in the extracellular matrix. These glycoproteins are known for their molecular weight of approximately 100 kDa and their modular structure. The *FBLN1* gene, which encodes fibulin-1, was the initial member of the fibulin family to be identified. It is situated on the long arm of human chromosome 22 (*22q13.3*). The protein is commonly found in the extracellular matrix of various organs, particularly in proximity to membranes, elastic fibers, and other connective tissue structures. This distribution implies its involvement in the process of matrix remodeling [8]. Fibulin-1 has been detected in the plasma and has been discovered in embryonic fetuses during the early stages of development [9]. Tissue-specific oligonucleotide arrays were used on both human and animal samples [10] to show that the levels of fibulin-1 mRNA and protein go up a lot in the placenta. Chemerin is classified as an adipokine, a group of proteins secreted by adipose tissue. It is composed of 163 amino acids and undergoes activation by the action of a serine protease enzyme, resulting in the formation of the biologically active form of chemerin [11]. The gene in interest was first identified in 1997 and subsequently acknowledged in 2007 [12], identified first in pre-psoriasis dermatologists [13], and the chemerin hormone is linked to various disorders, including cardiovascular disease. Chemerin receptor transcripts were mostly discovered in the spleen, placenta, lymph glands, pituitary gland, liver, and arthritis patients' synovial fluid pools. White blood cells (WBC) did not express it [14]. High chemerin levels are linked to ulcerative colitis, hepatitis, and polycystic ovarian syndrome [15]. A positive link has been observed between the levels of chemerin and the occurrence of polycystic ovarian syndrome [16]. Omentin-1 is a glycoprotein consisting of 296 amino acids and N-linked oligosaccharides. Its fundamental structural component is a homotrimer with a molecular weight of 120 kDa, wherein 40 kDa polypeptides are interconnected through disulfide bonds. There exists a correlation between the aforementioned condition and obesity, type 2 diabetes, the metabolic syndrome, and PCOS [17]. The adipokines, which are mostly expressed in the visceral (omental) adipose tissue and to a far lower degree in the subcutaneous adipose tissue, are detectable in human serum [18]. The present study aims to evaluate the influence of fibulin-1 as a new marker for PCOS and if the levels of chemerin and omentien-1 are affected by infertility and PCOS.

METHODS

Study design and patient selection

The samples were collected between October 2022 and March 2023 from patients who attended Al-Yarmook teaching hospital, and approval of the study protocol was obtained from the Iraqi Ministry of Health and the Ministry of Higher Education and Scientific Research, Al-Nahrain University, College of Science. Blood samples were obtained from all participants and kept at -20°C until the analysis was done. 150 women were participating in our study, including 50 infertile women with PCOS, 60 women with PCOS only, and 40 apparently normal, healthy women considered a control group.

Inclusion and exclusion criteria

Women aged between 20 and 40 who have no other endocrine disorders were included. Pregnant women and those with other health problems such as hypertension, kidney disease, a history of type II diabetes mellitus, or using ovulation-inducing medications were excluded.

Analysis of markers

To determine the amount of Feutin-A in serum samples, the ELISA Kit from Abcam uses an enzyme-linked immunosorbent assay (ELISA) methodology. The electro-chemiluminescence immunoassay technique was utilized to evaluate the concentrations of blood TC, HDL, TG, PROG and PRL. The Cobas e 411 system, which was jointly created by Roche and Hitachi Companies, was utilized for this specific objective.

Statistical analysis

Statistical analysis was conducted using GraphPad Prism, version 8.0.2 (GraphPad Software, San Diego, California, USA). The mean ± standard deviation (SD) was used to express the descriptive analysis of biochemical parameters. The research utilized parametric variables and conducted comparisons using the Mann-Whitney U test. A regression analysis was conducted to investigate the association between variables among women diagnosed with PCOS and infertility, as well as a control group. Pearson's correlation coefficient was employed for this purpose. A statistically significant result is considered at p-value<0.05.

RESULTS

Table 1 shows the comparison of the studied parameters between control, PCOS and infertile women with PCOS. There were non-significant changes observed in age (p=0.0578) and BMI (p=0.2970) between the control, PCOS and infertile women with PCOS groups.

Table 1: Descriptive data of fibulin-1, chemerin, omentin-1 levels and other parameters in PCOS, PCOS infertility and control

Parameters	Control	PCOS	PCOS with infertility	p-value
BMI (Kg/m^2)	23.95±2.24	24.11±2.77	24.92±2.82	0.2970
Age (year)	27.55±4.09	28.70±5.09	30.10±5.60	0.0578
Fibulin-1 (ng/mL)	209.7±37.24	365.0±70.53	404.0±70.93	<0.0001
Chemerin (ng/mL)	165.8±39.61	364.7±86.30	451.9±104.5	<0.0001
Omentin-1(ng/mL)	10.07±1.53	7.56±1.75	6.998±0.94	<0.0001
TC (mg/dL)	175.7±27.09	185.8±27.03	227.5±26.98	<0.0001
HDL-c (mg/dL)	76.13±25.29	66.65±30.34	46.13±12.56	<0.0001
TG (mg/dL)	105.7±21.81	111.6±26.57	167.7±24.06	<0.0001
PRL (pg/ml)	9.55±3.02	14.18±3.31	18.18±4.034	<0.0001
PROG (ng/ml)	1.25±0.42	0.854±0.369	0.76±0.43	<0.0001

Values were presented as mean±SD; BMI: body mass index; TC: total cholesterol; HDL-c: high-density lipoprotein cholesterol; TG: triglycerides; PRL: prolactin; PROG: progesteron.

Figures 1, 2 and 3 showed that there is a significant decrease in omentin-1 with a significant increase in fibulin-1 and chemerin.

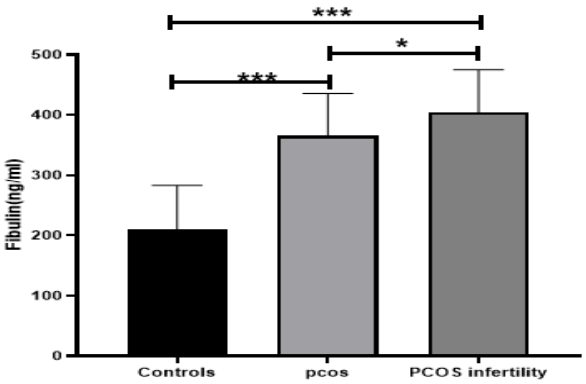

Figure 1: Serum levels of Fibulin-1 in controls, PCOS and PCOS infertility. *p<0.05; ***p<0.01.

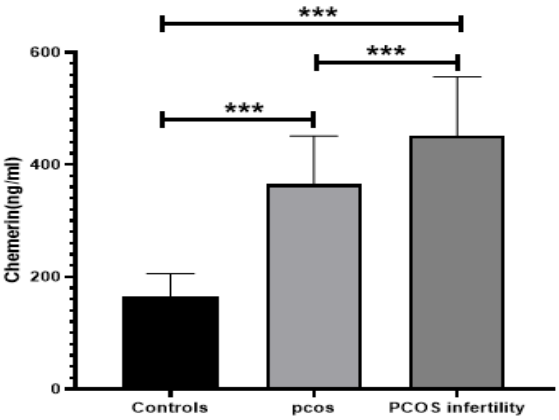

Figure 2: Serum levels of Chemerin in Controls, PCOS and PCOS infertility. ***p<0.01.

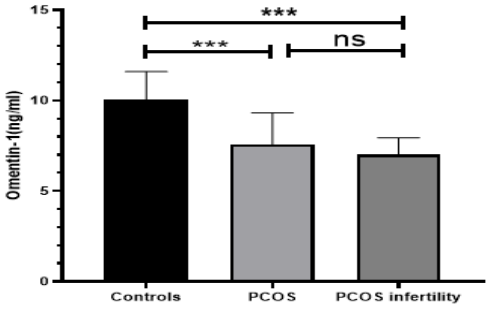

Figure 3: Serum levels of omentin-1 in controls, PCOS and PCOS infertility. ***p<0.01; ns: p>0.05.

A comparison study of the three groups also showed that there were statistically significant changes in levels for both the PCOS group compared to the control group and the PCOS infertility group compared to the control group (p<0.0001). Pearson correlation analysis was used to examine the associations between biomarkers of PCOS in both the PCOS and PCOS infertility groups. Tables 2, 3, and 4 show the correlations between the fibulin-1, chemerin and omentin-1 serum levels and other study variables in both PCOS groups. Table 2 shows that fibulin-1 in PCOS has a positive correlation with BMI, HDL, PRL, RROG and chemerin, while TC, TG and omentin-1

have a negative correlation, while PCOS and infertility show a positive correlation with HDL, TG, PRL and chemerin and a negative correlation with omentin-1, BMI, TC and PROG.

Table 2: Correlation of serum fibulin-1 levels in PCOS and PCOS-infertile women with other biochemical and hormone markers

Parameters	Fibulin-1 PCOS		Fibulin-1 Infertile PCOS	
	r	*P*	*r*	*p*
BMI(Kg/m^2)	0.163	0.374	-0.065	0.714
TC (mg/dL)	-0.327	0.030	-0.064	0.676
HDL (mg/dL)	0.178	0.271	0.129	0.429
TG (mg/dL)	-0.209	0.174	0.275	0.065
PRL (pg/ml)	0.043	0.791	0.260	0.106
PROG (ng/ml)	0.122	0.453	-0.392	0.0124
Omentin-1 (ng/mL)	-0.216	0.160	-0.19	0.240
Chemerin(ng/mL)	0.13	0.402	0.020	0.897

r: Pearson's correlation coefficient; BMI: body mass index; TC: total cholesterol; HDL-c: high-density lipoprotein cholesterol; TG: triglycerides; PRL: prolactin; PROG: progesteron.

In Table 3, chemerin in PCOS was positively correlated with BMI, HDL, PRL, TC, TG, chemerin and omentin-1 and negatively correlated with PROG, while in infertile PCOS it shows a positive correlation with BMI, PROG, PRL, fibulin-1 and omentin-1 and a negative correlation with TC.

Table 3: Correlation of serum chemerin levels in PCOS and PCOS-infertile women with the other biochemical and hormone markers

Parameters	Chemerin PCOS		Chemerin Infertile PCOS	
	r	*p*	*r*	*p*
BMI (Kg/m^2)	0.310	0.084	0.196	0.267
TC (mg/dL)	0.091	0.553	-0.049	0.752
HDL (mg/dL)	0.039	0.812	0.179	0.268
TG (mg/dL)	0.124	0.419	0.195	0.199
PRL (pg/ml)	0.039	0.809	0.139	0.394
PROG (ng/ml)	-0.311	0.051	0.005	0.977
Omentin-1 (ng/mL)	0.130	0.402	0.020	0.897
Chemerin(ng/mL)	0.152	0.319	0.003	0.984

r: Pearson's correlation coefficient; BMI: body mass index; TC: total cholesterol; HDL-c: high-density lipoprotein cholesterol; TG: triglycerides; PRL: prolactin; PROG: progesteron.

Finally, Table 4 displayed that omentin-1 in PCOS has a positive correlation with BMI, TC, TG, PRL and chemerin and a negative correlation with HDL, PROG and fibulin-1, while in infertile PCOS it shows a positive correlation with BMI, TC, PRL and chemerin and a negative correlation with PROG, HDL, TG and fibulin-1.

DISCUSSION

In this study, compared to controls, PCOS and PCOS with infertility had higher levels of fibulin-1. These findings are consistent with the study conducted by Scarinci *et al*., which showed that individuals with PCOS had higher levels of fibulin-1 in comparison to the control group.

Table 4: Correlation of serum omentin-1 levels of PCOS and PCOS-infertile women with other biochemical and hormone markers

Parameters	Omentin-1 PCOS		Omentin-1 Infertile PCOS	
	r	*p*	*r*	*p*
BMI (Kg/m^2)	0.345	0.053	0.331	0.056
TC (mg/dL)	0.458	0.001	0.140	0.388
HDL (mg/dL)	-0.088	0.589	-0.003	0.983
TG (mg/dL)	0.054	0.723	-0.095	0.561
PRL (pg/ml)	0.017	0.916	0.136	0.403
PROG (ng/ml)	-0.331	0.037	-0.014	0.933
Omentin-1 (ng/mL)	-0.216	0.160	-0.190	0.240
Chemerin(ng/mL)	0.152	0.319	0.003	0.984

r: Pearson's correlation coefficient; BMI: body mass index; TC: total cholesterol; HDL-c: high-density lipoprotein cholesterol; TG: triglycerides; PRL: prolactin; PROG: progesteron.

The findings of this study lend additional credence to the theory that endothelium injury is a common occurrence in women with polycystic ovarian syndrome (PCOS). Fibulin-1 analysis, a recognized marker linked to endothelial and cardiovascular diseases, provides proof of this [19]. In our study, the PCOS group and the infertile PCOS group had higher levels of chemerin than the control group. Infertility with PCOS also results in a much greater amount of chemerin than PCOS alone. This result is consistent with the study of Ademoglu *et al*., which demonstrates that women with PCOS generally had greater serum chemerin levels than the control group. The authors do concede, nevertheless, that further research is needed to completely understand the precise physiological effects of elevated serum chemerin levels in PCOS [16]. The study findings are consistent with those of Halawa *et al*., who examined the levels of chemerin in women with PCOS and healthy women and discovered that the latter had significantly greater amounts, which they associated with insulin resistance [20]. Furthermore, Yang *et al*. found that chemerin was an adipokine that may cause IR and that infertile PCOS women had greater serum chemerin levels than controls [21]. Women with PCOS reported considerably greater serum chemerin levels than controls, indicating that those with PCOS and IR had higher serum chemerin levels than women without PCOS and IR. Moreover, serum chemerin levels were higher in PCOS with IR than in PCOS without IR [22]. Contrary to the current findings, Guvenc *et al*. evaluation of chemerin levels in both groups revealed no variations in serum chemerin levels between PCOS patients and healthy controls. The absence of a significant difference between the groups, however, may be explained by the exclusion of patients with IR from this study [23]. Additionally, PCOS patients showed slightly greater serum levels of chemerin than controls, according to Kort *et al*. [24]. It has been discovered that omentin-1 improves human adipocytes' sensitivity to insulin. Comparing the PCOS

group and the infertile PCOS group to the control group, our results show a decrease in omentin-1 levels. Compared to the PCOS subgroup with infertility, the PCOS group had a slightly higher concentration of omentien-1; however, this difference was not statistically significant. In line with the findings of a study by Mahde *et al*., these data demonstrate a significant drop in serum omentin-1 levels in PCOS infertile patients as compared to the control group. Additionally, assessment of insulin resistance (HOMA-IR), fasting insulin, and HOMA ß-cell are negatively correlated with plasma omentin-1 levels [25]. This shows that omentin-1 may be related to the body's sensitivity to insulin. Furthermore, compared to women without PCOS, individuals with PCOS had considerably decreased serum omentin-1 levels, according to a study by Orlik *et al*. Furthermore, it was demonstrated that variations in serum omentin-1 levels could be explained by estradiol, the LH/FSH ratio, the HOMA-IR, and the Free Androgen Index (FAI) [26]. In a different investigation, Choi *et al*. demonstrated that in PCOS patients as opposed to non-PCOS patients, postprandial hyperinsulinemia and hyperglycemia have a stronger effect on the decrease of omentin-1 levels. There is a substantial correlation between IR and glucose metabolism and omentin-1. Furthermore, there is proof that in PCOS patients, there are noteworthy correlations between decreased omentin-1 levels and androgen levels. The authors argue that the control of omentin-1 production in adipose tissue is influenced by multiple factors. Furthermore, they claim that in the context of PCOS, IR development may be influenced by elevated androgen levels and decreased omentin-1 levels in patients [27]. Kort *et al*. showed that PCOS patients had lower levels of omentin-1 than did the control group. They looked into the relationship between omentin-1 levels and other adipokines as well as other factors, but they were unable to find any meaningful relationships. It appears that the stromal vasculature in adipose tissue, rather than the adipocytes themselves, may be the cause of the reduced levels of omentin-1 in PCOS [24]. Their interpretation of our results differs from that of Alanya Tosun and colleagues. They show that, in comparison to the control group, those with PCOS have higher levels of omentin-1. Moreover, their research indicates that early-stage PCOS cases that manifest at a younger age had considerably higher serum omentin-1 levels. According to these results, omentin-1 may function in PCOS as a protective acute-phase reactant [28]. A major factor in PCOS and infertility is the lipid profile. The results of our analysis show that those with PCOS have somewhat higher levels of TC, TG, and HDL than those in the control group. This difference may be explained by the fact that the women in our study were of a normal weight. On the other hand, we found a significant increase in the levels of TC, TG, and HDL when comparing people with PCOS and infertility to those with PCOS alone and the control group. The results of this investigation are in line with those of Orio *et al*. [29], who showed that blood TC, LDL-C, HDL-C, and TG levels did not significantly differ between the PCOS and control groups. Sahin *et al*. conducted a different study in which they found no significant differences in plasma TC, LDL-C, HDL-C, and TG levels between a group of 50 PCOS patients and a control group of 40 individuals matched for age and BMI [30]. According to Dastorani *et al*., PCOS and infertile patients may have worsening lipid profiles as a result of increased androgen and insulin levels. Reproduction and inflammation are impacted by byproduct fatty acids. Vitamin D can reduce the formation of PTH and improve insulin sensitivity, which can lower TC and LDL-c. Insulin also reduces TC and LDL-c and increases HMG-CoA reductase activity, which decreases the manufacture of cholesterol [31]. High TC levels in PCOS women who are infertile could be caused by abnormalities in TC absorption, cross-consumption of stored fat, or the body's reliance on alternative energy sources [32]. Furthermore, elevated TC levels are linked to IR, low HDL-C levels, and the risk of atherosclerosis [33]. It is believed that lipid disorders contribute to female reproduction in both primary and secondary infertility. The granulosa and thecal cells of the reproductive organs produce steroid hormones, using cholesterol as a substrate for steroidogenesis. When it comes to the transport of cholesterol to ovarian tissue, both HDL-C and LDL-C are essential [34]. Variations in the endometrium's lipid content may have a detrimental effect on the endometrium's receptivity and the success of an early embryo's implantation [35]. In our study, we found that progesterone levels considerably fell in PCOS cases with infertility when compared to control, and in PCOS cases without infertility when compared to control. This was due to progesterone levels being lowered as a result of anovulation or oligo ovulation. Our findings that progesterone levels in PCOS patients declined dramatically when compared to the control group are also supported by Kabil Kucur *et al*. [36]. Gulhan *et al*. demonstrated, in contrast to our findings, that progesterone levels were not statistically significant in either the PCOS or control groups [37]. Furthermore, non-significant differences between PCOS and the control group were demonstrated by Tan *et al*. [38]. Moreover, research indicates that more than 50% of women who present with amenorrhea and agalactorrhea also have elevated prolactin levels. Compared to the control group, we found that those with PCOS and infertile PCOS had greater prolactin concentrations during our analysis. The results of this investigation showed that prolactin levels were significantly higher in PCOS patients than in the control group. In this context, it has been shown that women with PCOS and infertility had significantly higher prolactin levels than those with PCOS alone. Since the results of Abdelsalam *et al*. showed a link between hypothyroidism and PCOS, they concurred with the results of this investigation. They also noted that in the same set of people, this hypothyroidism may result in hyperprolactinemia. These recommend that in order to identify the cause of their hyperprolactinemia, people with

PCOS and hyperprolactinemia should have an evaluation of their thyroid function [39]. Additionally, Hassan (2020) showed a substantial rise in prolactin levels in infertile patients with PCOS compared to a non-PCOS control group, which is consistent with our own findings. The author added that although persistent hyperestrogenemia in PCOS has been suggested as a potential trigger for prolactin production, the exact source of the elevated prolactin levels is still unknown. Approximately 5–30% of people with PCOS had a small increase in blood prolactin levels (range from 20 to 40 ng/dl) [40]. Our results are consistent with another study by Esmaeilzadeh *et al*., which found that blood prolactin levels are higher in infertile PCOS patients than in healthy individuals. This could be explained by the fact that several features of PCOS are associated with diminished hypothalamic dopaminergic activity, which results in the elevated levels of TSH, FSH, and LH ratios [41]. A study performed by Yang *et al*., in contrast, showed that infertile women with PCOS had significantly lower serum prolactin levels than women without PCOS. Additionally, they offered proof that infertile women with PCOS who had low serum prolactin levels within the normal range are more likely to have insulin resistance and beta-cell malfunction [42]. Szosland et al., on the other hand, offer a different perspective, arguing that blood prolactin levels in PCOS patients are within normal limits. They maintained that any association between higher serum prolactin levels and PCOS is merely coincidental [43].

Conclusion

The increased level of fibulin-1 may be a new marker for PCOS and infertility. Chemerin shows a high level in both infertile PCOS and PCOS women, while omentin-1 shows a low level in both infertile PCOS and PCOS women.

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Conflict of interests

No conflict of interest was declared by the authors

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

RFERENCES

1. Kadium TE, Alrubaie A, Ghanim SAM. The Link between serum omentin level and insulin resistance biomarkers, lipid Profile, and atherogenic indices in Iraqi obese patients. *Baghdad Sci J*. 2023;20(1):0074. doi: 10.21123/bsj.2022.6535.
2. Hajam YA, Kumar R, Thakur D, Rai S, (Eds.), Polycystic ovarian syndrome (PCOS): Signs, symptoms, epidemiology, environmental stress, management strategies and current therapies. Herbal Medicine Applications for Polycystic Ovarian Syndrome: CRC Press; 2023, p. 1-17.
3. Lomteva S, Shkurat T, Bugrimova E, Zolotykh O, Alexandrova A, Karantysh G. Violation of the hormonal spectrum in polycystic ovaries in combination with insulin resistance. What is the trigger: Insulin resistance or polycystic ovary disease? *Baghdad Sci J*. 2022;19(5):0990. doi: 10.21123/bsj.2022.6317.
4. Tang Z, Guan J, Mao JH, Han L, Zhang JJ, Chen R, et al. Quantitative risk-benefit profiles of oral contraceptives, insulin sensitizers and antiandrogens for women with polycystic ovary syndrome: a model-based meta-analysis. *Eur J Pharm Sci*. 2023:106577. doi: 10.1016/j.ejps.2023.106577.
5. Teut M, van Haselen RA, Rutten L, Lamba CD, Bleul G, Ulbrich-Zürni S. Case reporting in homeopathy-An overview of guidelines and scientific tools. *Homeopathy*. 2022;111(1):2-9. doi: 10.1055/s-0041-1731313.
6. Rajashekar S, Ravindran SG, Kakarla M, Gambo MA, Salama MY, Ismail NH, et al. Spironolactone versus oral contraceptive pills in the treatment of adolescent polycystic ovarian syndrome: A systematic review. *Cureus*. 2022;14(5). doi: 10.7759/cureus.25340.
7. Vanders RL, Gomez HM, Hsu AC, Daly K, Wark PA, Horvat JC, et al. Inflammatory and antiviral responses to influenza A virus infection are dysregulated in pregnant mice with allergic airway disease. *Am J Physiol Lung Cell Mol Physiol*. 2023;325(3):L385-L398. doi: 10.1152/ajplung.00232.2022.
8. Kobayashi N, Kostka Gn, Garbe H, Keene DR, Bächinger HP, Hanisch FG, et al. A comparative analysis of the fibulin protein family: biochemical characterization, binding interactions, and tissue localization. *J Biol Chem*. 2007;282(16):11805-11816. doi: 10.1074/jbc.M611029200.
9. Orvik AB, Andersen MR, Pedersen L, Ritz C, Stender S, Szecsi PB. Plasma fibulin-1 levels during pregnancy and delivery: a longitudinal observational study. *BMC Pregnancy Childbirth*. 2021;21(1):1-10. doi: 10.1186/s12884-021-04110-y.
10. Karlsson M, Sjöstedt E, Oksvold P, Sivertsson Å, Huang J, Álvez MB, et al. Genome-wide annotation of protein-coding genes in pig. *BMC Biol*. 2022;20(1):1-18. doi: 10.1186/s12915-022-01229-y.
11. Cătoi AF, Suciu Ş, PÂrvu AE, Copăescu C, Galea RF, Buzoianu AD, et al. Increased chemerin and decreased omentin-1 levels in morbidly obese patients are correlated with insulin resistance, oxidative stress and chronic inflammation. *Clujul Med*. 2014;87(1):19. doi: 10.15386/cjm.2014.8872.871.afc1.
12. Nagpal S, Patel S, Jacobe H, DiSepio D, Ghosn C, Malhotra M, et al. Tazarotene-induced gene 2 (TIG2), a novel retinoid-responsive gene in skin. *J Investig Dermatol*. 1997;109(1):91-95. doi: 10.1111/1523-1747.ep12276660.
13. Abdulwahed AMH, Alkanaani MIM, Alsamarrai AHJ, Hamad MAM, Dakheel AH, Ahmed TY, AL-Samarraie MQ. Determination of some visfatin hormone level and lipid profilein some breast cancer patients in Samarra city. *Ann Trop Med Pub Health*. 2020;23:S420. doi: 10.36295/ASRO.2020.23134.
14. Habib HA, Rahaem YA, AL-Khalid IMM. Knowledge, attitude and practice regarding obesity management among family and non-family physicians working in primary health care centers in Baghdad. *Iraqi Postgrad Med J*. 2012;10(4):7.
15. Toulany J. Development of a chemokine-like receptor 1 bioassay to study the impact of obesity on active chemerin production in obese humans. MSc theses, Dalhousie University Halifax, Nova Scotia December 2014.
16. 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;66(6):535-542. PMID: 25373013.
17. Barker G, Lim R, Georgiou HM, Lappas M. Omentin-1 is decreased in maternal plasma, placenta and adipose tissue of women with pre-existing obesity. *PLoS One*. 2012;7(8):e42943. doi: 10.1371/journal.pone.0042943.
18. Kruszewska J, Laudy-Wiaderny H, Kunicki M. Review of novel potential insulin resistance biomarkers in PCOS patients—The debate is still open. *Int J Environ Res Pub Health*. 2022;19(4):2099. doi: 10.3390/ijerph19042099.
19. Scarinci E, Tropea A, Russo G, Notaristefano G, Messana C, Alesiani O, et al. Increased fibulin-1 plasma levels in polycystic ovary syndrome (PCOS) patients: possible contribution to the link between PCOS and cardiovascular risk. *J Endocrinol Investig*. 2019;42:91-96. doi: 10.1007/s40618-018-0891-3.
20. Halawa MR, El Baky RSA, Eid YM, Nasr MS, Taha BM, Hendawy LMA. Chemerin level in a sample of Egyptian females with PCOS and its relation to insulin resistance. *Egypt J Intern Med*. 2020;32:1-5. doi; 10.1186/s43162-020-00019-8.
21. Yang X, Quan X, Lan Y, Wei Q, Ye J, Yin X, et al. Serum chemerin level in women with PCOS and its relation with the risk of spontaneous abortion. *Gynecol Endocrinol*. 2018;34(10):864-867. doi: 10.1080/09513590.2018.1462316.
22. Mansoori A, Amoochi-Foroushani G, Zilaee M, Hosseini SA, Azhdari M. Serum and follicular fluid chemerin and chemerin mRNA expression in women with polycystic ovary syndrome: Systematic review and meta-analysis. *Endocrinol Diabet Metab*. 2022;5(1):e00307. doi: 10.1002/edm2.307.
23. Guvenc Y, Var A, Goker A, Kuscu NK. Assessment of serum chemerin, vaspin and omentin-1 levels in patients with polycystic ovary syndrome. *J Int Med Res*. 2016;44(4):796-805. doi: 10.1177/0300060516645421.
24. Kort DH, Kostolias A, Sullivan C, Lobo RA. Chemerin as a marker of body fat and insulin resistance in women with polycystic ovary syndrome. *Gynecol Endocrinol*. 2015;31(2):152-155. doi; 10.3109/09513590.2014.968547.
25. Mahde A, Shaker M, Al-Mashhadani Z. Study of omentin1 and other adipokines and hormones in PCOS patients. *Oman Med J*. 2009;24(2):108. doi: 10.5001%2Fomj.2009.25.
26. Orlik B, Madej P, Owczarek A, Skałba P, Chudek J, Olszanecka-Glinianowicz M. Plasma omentin and adiponectin levels as markers of adipose tissue dysfunction in normal weight and obese women with polycystic ovary syndrome. *Clin Endocrinol*. 2014;81(4):529-535. doi: 10.1111/cen.12381.
27. Choi JH, Rhee EJ, Kim KH, Woo HY, Lee WY, Sung KC. Plasma omentin-1 levels are reduced in non-obese women with normal glucose tolerance and polycystic ovary syndrome. *Eur J Endocrinol*. 2011;165(5):789-796. doi: 10.1530/eje-11-0375.
28. Alanya Tosun Ş, Gurbuz T, Cebi A, Tosun A, Gokmen O, Usta M. Association of increased levels of omentin-1 and carotid intima-media thickness with early signs of cardiovascular risk in patients with polycystic ovary syndrome: A prospective case control study. *J Obstetr Gynaecol Res*. 2022;48(1):169-177. doi: 10.1111/jog.15077.
29. Orio F, Palomba S, Cascella T, De Simone B, Di Biase S, Russo T, et al. Early impairment of endothelial structure and function in young normal-weight women with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2004;89(9):4588-4593. doi: 10.1210/jcem.89.11.9998.
30. Sahin S, Eroglu M, Selcuk S, Turkgeldi L, Kozali S, Davutoglu S, et al. Intrinsic factors rather than vitamin D deficiency are related to insulin resistance in lean women with polycystic ovary syndrome. *Eur Rev Med Pharmacol Sci*. 2014;18(19): 2851-2856. PMID: 25339479.
31. Dastorani M, Aghadavod E, Mirhosseini N, Foroozanfard F, Zadeh Modarres S, Amiri Siavashani M, et al. The effects of vitamin D supplementation on metabolic profiles and gene expression of insulin and lipid metabolism in infertile polycystic ovary syndrome candidates for in vitro fertilization. *Reprod Biol Endocrinol*. 2018;16:1-7. doi: 10.1186/s12958-018-0413-3.
32. Nofer JR, Kehrel B, Fobker M, Levkau B, Assmann G, von Eckardstei A. HDL and arteriosclerosis: beyond reverse cholesterol transport. *Atherosclerosis*. 2002;161(1):1-16. doi: 10.1016/S0021-9150(01)00651-7.
33. Tilg H, Moschen AR. Inflammatory mechanisms in the regulation of insulin resistance. *Mol Med*. 2008;14:222-231. doi: 10.1136/gutjnl-2014-306928.
34. Huang Q, Liu Y, Yang Z, Xie Y, Mo Z. The effects of cholesterol metabolism on follicular development and ovarian function. Curr Mol Med. 2019;19(10):719-730. doi: 10.2174/1566524019666190916155004.
35. Li J, Gao Y, Guan L, Zhang H, Chen P, Gong X, et al. Lipid profiling of peri-implantation endometrium in patients with premature progesterone rise in the late follicular phase. *J Clin Endocrinol Metab*. 2019;104(11):5555-5565. doi: 10.1210/clinem/dgz179.
36. Kabil Kucur S, Kurek Eken M, Sanli I, Kutlu T, Bilgic BE, Altuntas ŞL, et al. Predictive value of serum and follicular fluid chemerin concentrations during assisted reproductive cycles in women with polycystic ovary syndrome. *Gynecol Endocrinol*. 2021;37(9):814-818. doi: 10.1080/09513590.2021.1937100.
37. Gulhan I, Bozkaya G, Oztekin D, Uyar I, Kebapcilar AG, Pamuk B. Serum fetuin-A levels in women with polycystic ovary syndrome. *Arch Gynecol Obstetr*. 2012;286:1473-1476. doi: 10.1007/s00404-012-2494-0.
38. Tan BK, Adya R, Farhatullah S, Lewandowski KC, O'Hare P, Lehnert H, et al. Omentin-1, a novel adipokine, is decreased in overweight insulin-resistant women with polycystic ovary syndrome: ex vivo and in vivo regulation of omentin-1 by insulin and glucose. *Diabetes*. 2008;57(4):801-808. doi: 10.2337/db07-0990.
39. Abdelsalam KEA, Ibrahim W. Relationship between TSH, T4, T3 and prolactin in overweight and lean Sudanese PCOS patients. *Int J Biomed Res*. 2015;6(2):108-112. doi: 10.7439/ijbr.
40. Hassan MF. The frequency of elevated prolactin level in polycystic pvary syndrome women (PCOS) and its effect on pregnancy rate. *Glob J Pub Health Med*. 2020;2(1):109-117. doi: 10.37557/gjphm.v2i1.28.
41. Esmaeilzadeh, S., et al., *Association between endometriosis and hyperprolactinemia in infertile women*. Iranian journal of reproductive medicine, 2015. **13**(3): p. 155.
42. Yang H, Lin J, Li H, Liu Z, Chen X, Chen Q. Prolactin is associated with insulin resistance and beta-cell dysfunction in infertile women with polycystic ovary syndrome. *Front Endocrinol*. 2021;12:571229. doi: 10.3389/fendo.2021.571229.
43. Szosland K, Pawlowicz P, Lewiński A. Prolactin secretion in polycystic ovary syndrome (PCOS). *Neuro Endocrinol Lett*. 2015;36(1):53-58. PMID: 25789595.