Possible Association Between Vaspin Serum Levels and C-Reactive Protein in Obese Women with Polycystic Ovarian Syndrome

Aya Fawzi Talib[1] ⓘ, Shahad Sabah Khalid[2*] ⓘ, Mohammed A. Abd[2] ⓘ

[1]College of Pharmacy, Clinical Pharmacy Department, Uruk University, Baghdad, Iraq.
[2]Department of Pharmacy, Al Nukhba University, Baghdad, Iraq.
*Correspondence to: Shahad Sabah Khalid (E-mail: s.sabahph@alnukhba.edu.iq)
(Submitted: 01 June 2024 – Revised version received: 06 June 2024 – Accepted: 20 June 2024 – Published online: 26 June 2024)

Abstract

Objective: To investigate the levels of vaspin and C-reactive protein in women with polycystic ovarian syndrome (PCOS) and to assess their potential as diagnostic markers for the condition.

Methods: Ninety adult women were involved in the study, fifty of whom were obese women diagnosed with PCOS, while forty women served as healthy controls in an observational, case-control study. Blood samples were obtained from the participants, and all of them were questioned by the researcher. Vaspin and C-reactive protein serum levels were measured using enzyme-linked immunosorbent assay specialized kits.

Results: The study found a significant increase in vaspin and C-reactive protein serum levels in women in the PCOS group compared with controls, with P-values of <0.000 and 0.006, respectively. Vaspin serum level showed an AUC of 0.835, indicating it is a very good diagnostic marker for PCOS, while C-reactive protein had an AUC of 0.635, making it a moderate diagnostic marker for PCOS. The study also found a significant correlation between vaspin (pg/ml) and C-reactive protein (mg/l) with a P-value of 0.006.

Conclusion: The study found a significant increase in vaspin (pg/ml) and C-reactive protein (mg/l) serum levels in females with PCOS compared to control groups, with a significant positive correlation between the two biomarkers in PCOS. This suggests that vaspin and C-reactive protein may serve as useful diagnostic markers for PCOS.

Keywords: PCOS, vaspin, C-reactive protein

Introduction

The diverse set of illnesses known as PCOS affects women who are fertile rather frequently. Polycystic ovarian syndrome, which affects 6–8% of women throughout the reproductive age, is the most prevalent endocrine disorder in the reproductive age.[1] The origin of PCOS is still unknown, but behavioral, environmental, and genetic variables have been linked to its development. Nevertheless, PCOS patients have a four-fold increased risk of metabolic syndrome compared to non-PCOS individuals. The majority of doctors concur that a woman with hirsutism, irregular menstruation cycles, obesity, and a characteristic ovarian morphology can be clinically diagnosed with PCOS.[2]

Vaspin has been identified as a member of the serine protease inhibitor family (serpin) originating from visceral adipose tissue. Expression of the serpin mRNA was observed in the skin, stomach, liver, and visceral adipose tissue.[3] Vaspin circulating level markedly increases in obese individuals.[4] Furthermore, it has been documented that vaspin has anti-inflammatory properties since this adipokine reduces the amount of TNFα in the blood. proving that vaspin inhibits the production of proinflammatory molecules in vascular endothelial cells that are triggered by cytokines, Vaspin may therefore play a role in the etiology of obesity and PCOS.[5]

Acute phase protein (APP) from the liver is generated in reaction to IL-6, which is secreted by activated cells like adipocytes and macrophages. Consequently, a range of health problems, such as infertility, cardiovascular disease (CVD), and diabetes, are more likely to affect women with PCOS.[6]

The main objective of the current study was to determine vaspin and C-reactive protein concentrations in obese PCOS patients and healthy women and to examine the possible correlation between these two markers.

Method

Study Design and Setting

Ninety females were included in the study, fifty of them were obese with PCOS compared to forty obese females healthy controls in an observational, case-control study. This research was performed at a Specialized fertility center at a Middle East private hospital in Baghdad/Iraq, from February 2024 to May 2024.

Sample Selection

Inclusion criteria: Females of reproductive age (18–40 years old), obese BMI > 30, diagnosed with PCOS according to Rotterdam E. Revised (2003),[7] willing to participate, exclusion criteria; pregnancy, heart disease, thyroid dysfunction, cancer, high blood pressure, kidney failure, and other endocrine disorders For the previous two months, none of the patients had taken any kind of steroid-containing medication, including glucocorticoids, anti-obesity medications, ovulation induction medicines, or oral contraceptives.

Ethical consideration: This work was performed according to the Helsinki II Declaration.[8] The ethics committee of the Uruk University/College of Pharmacy (ethics board approval code:8).

Data Collection and Outcome Measurements

The subjects were asked questions by the researcher and blood samples were taken under similar circumstances. Patient case

files or one-on-one interviews were used to obtain direct data from patients. Before registration, each participant completed a consent form granting access to their case file and all pertinent recorded information, such as name, age, diseases, and medication history. Five milliliters of blood from each participant were obtained; the blood was then put in a tube and centrifuged for ten to fifteen minutes. Enzyme-linked immunosorbent assay analysis was used to measure the levels of Vaspin and C-reactive protein using participant serum and specialized kits.

Statistical Analysis

Version 27 of Microsoft Windows software (ID: SCR_016479) was used to conduct the statistical study. The mean is the display used for descriptive statistics. Descriptive data are shown as mean ± SD. The unpaired T-test was used to compare the females with PCOS and healthy outcomes of normally distributed variables. Pearson's chi-squared test was employed to investigate the correlations between parameters for categorical variables. The receiver operating characteristic (ROC) curve was utilized to determine the optimal cut-off value in terms of specificity, sensitivity, and area under the curve (AUC).

Results

A case-control study with 90 females involved, 50 female patients who had been diagnosed previously with PCOS, and 40 healthy participants as a control group. There were no markable differences in weight, height, age, and BMI between the two groups, Table 1.

The study showed a significant elevate in vaspin (pg/ml) serum levels in females with PCOS when compared with controls with a P-value of < 0.000, and the descriptive statistic (mean ± SD) was 434.41 ± 227.21 (pg/ml) while for control was 7.833 ± 4.829 (pg/ml), also significant elevate in C-reactive protein (mg/l) with a P-value of 0.006, and the descriptive statistic (mean ± SD) was 20.2667 ± 22.067 (mg/ml) while for control was 7.833 ± 4.829 (mg/ml), Table 2.

Vaspin (pg/ml) and C-reactive protein (mg/l) had an AUC of 0.835 and 0.635 respectively which suggested vaspin (pg/ml) as a very good diagnostic marker while C-reactive protein (mg/l) as medium diagnostic marker for PCOS in female patients, with optimal cut-off value of 241.27 pg/ml and sensitivity and specificity of 80% and 72% respectively while for C-reactive protein an optimal cut-off value of 5.555 mg/l and sensitivity and specificity of 73% and 45% respectively, Table 3 and Figure 1.

The current study found a significant correlation between vaspin (pg/ml) and C-reactive protein (mg/l) with P-value 0.006 as shown in Table 4.

Discussion

The results of this work showed that vaspin serum level increase in females with PCOS compared to healthy control in contrast to two other studies where showed no differences in vaspin serum level in females with PCOS compared to non-PCOS females.[9,10]

The results of this work showed that C-reactive protein serum level increase in females with PCOS compared to

Table 2. **C-reactive protein and Vaspin serum level between the two groups**

Parameter	Group	N	Mean ± SD	P-value
C-reactive protein (mg/l)	Patient	50	20.2667 ± 22.067	*0.006
	Control	40	7.833 ± 4.829	
Vaspin (pg/ml)	Patient	50	434.41 ± 227.21	*<0.000
	Control	40	203.48 ± 166.19	

*P-value<0.05 significant.

Table 3. **AUC and ROC for Vaspin and C-reactive protein serum level in the two groups**

Parameter	AUC	P-value	Optimal cut-off point	SN	SP
Vaspin (pg/ml)	0.835	*<0.000	241.27	80%	72%
C-reactive protein (mg/l)	0.635	*0.0083	5.555	73%	45%

*P-value<0.05 significant.
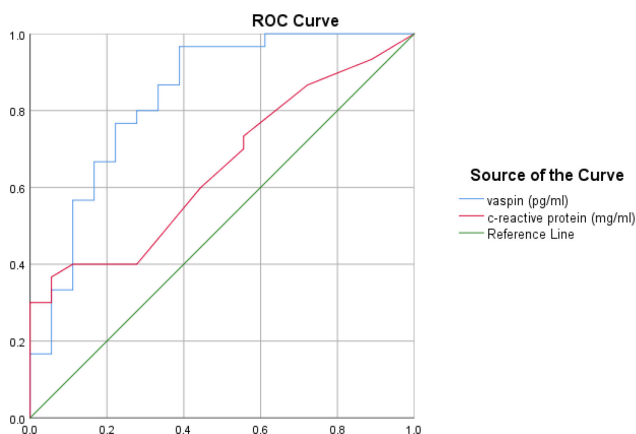
Fig. 1 **ROC for Vaspin and C-reactive protein.**

Table 1. **Participants characteristic**

Parameter	Group	N	Mean ± SD	P-value
Weight (Kg)	Patient	50	89.462 ± 19.88	0.654
	Control	40	84.943 ± 10.43	
Height (cm)	Patient	50	165.13 ± 2.13	0.432
	Control	40	160.34 ± 19.77	
Age (year)	Patient	50	29.92 ± 2.05	0.90
	Control	40	29.23 ± 4.33	
BMI (kg/m²)	Patient	50	33.10 ± 12.10	0.71
	Control	40	31.30 ± 9.12	

Table 4. **Correlation between Vaspin and C-reactive protein**

Parameter	Vaspin (pg/ml)	
	r-Pearson	P-value
C-reactive protein (mg/l)	0.329	*0.006

*P-value<0.05 significant; r, Pearson correlation coefficient.

Original
A.F. Talib et al.
Vaspin and C-reactive Protein Serum Level in Women with Polycystic Ovarian Syndrome

healthy control and this finding may related to raise the chance of developing certain illnesses, such as diabetes, cardiovascular disease (CVD), and infertility, Women with PCOS are also shown to exhibit higher levels of chronic subclinical inflammation, which is commonly clinically measured by measuring serum levels of C reactive protein (CRP). This finding may be related to the constellation of endocrine and metabolic abnormalities that these women face.[11] The finding of this study agreed with a meta-analysis of 31 studies concluded that systemic CRP levels are 96% higher in women with PCOS compared with control women.[12]

Diamanti E et al. had proposed that PCOS is associated with chronic low-grade inflammation, specifically CRP. More precisely, compared to their age- and BMI-matched, normal-ovulating, non-hyperandrogenic contemporaries, women with PCOS had statistically significantly higher CRP concentrations. These results validate the information provided by numerous studies assessing diverse groups of women with PCOS.[13]

The main limitations of the study are the small sizes of study groups.

Conclusion

In that study, the vaspin (pg/ml) and C-reactive protein (mg/l) serum levels had been measured in females with PCOS, and correlation between them had been investigated, the study found significant increase in vaspin (pg/ml) and C-reactive protein (mg/l) serum levels in females with PCOS compared to control groups, with significant positive correlation between the two biomarkers in PCOS.

Acknowledgment

Conflict of Interest

None.

References

1. Leon LIR, Mayrin J V. Polycystic ovarian disease (Stein-Leventhal syndrome). Stat Pearls [Internet] Stat Pearls Publ. 2018.
2. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004;89(6):2548–56.
3. Klöting N, Kovacs P, Kern M, Heiker JT, Fasshauer M, Schön MR, et al. Central vaspin administration acutely reduces food intake and has sustained blood glucose-lowering effects. Diabetologia. 2011;54:1819–23.
4. Klöting N, Berndt J, Kralisch S, Kovacs P, Fasshauer M, Schön MR, et al. Vaspin gene expression in human adipose tissue: association with obesity and type 2 diabetes. Biochem Biophys Res Commun. 2006;339(1):430–6.
5. Jung CH, Lee MJ, Kang YM, Lee Y La, Yoon HK, Kang SW, et al. Vaspin inhibits cytokine-induced nuclear factor-kappa B activation and adhesion molecule expression via AMP-activated protein kinase activation in vascular endothelial cells. Cardiovasc Diabetol. 2014;13:1–11.
6. Marciniak A, Nawrocka-Rutkowska J, Brodowska A, Wiśniewska B, Starczewski A. Cardiovascular system diseases in patients with polycystic ovary syndrome-the role of inflammation process in this pathology and possibility of early diagnosis and prevention. Ann Agric Environ Med. 2016;23(4).
7. Rotterdam E. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19–25.
8. Giordano S. The 2008 Declaration of Helsinki: some reflections. J Med Ethics. 2010;36(10):598–603.
9. Akbarzadeh S, Ghasemi S, Kalantarhormozi M, Nabipour I, Abbasi F, Aminfar A, et al. Relationship among plasma adipokines, insulin and androgens level as well as biochemical glycemic and lipidemic markers with incidence of PCOS in women with normal BMI. Gynecol Endocrinol. 2012;28(7):521–4.
10. Cekmez F, Cekmez Y, Pirgon Ö, Canpolat FE, Aydinöz S, Ipcioglu OM, et al. Evaluation of new adipocytokines and insulin resistance in adolescents with polycystic ovary syndrome. Eur Cytokine Netw. 2011;22(1):32–7.
11. Shorakae S, Teede H, de Courten B, Lambert G, Boyle J, Moran LJ. The emerging role of chronic low-grade inflammation in the pathophysiology of polycystic ovary syndrome. In: Seminars in reproductive medicine. Thieme Medical Publishers; 2015. p. 257–69.
12. Escobar-Morreale HF, Luque-Ramírez M, González F. Circulating inflammatory markers in polycystic ovary syndrome: a systematic review and metaanalysis. Fertil Steril. 2011;95(3):1048–58.
13. Diamanti-Kandarakis E, Paterakis T, Alexandraki K, Piperi C, Aessopos A, Katsikis I, et al. Indices of low-grade chronic inflammation in polycystic ovary syndrome and the beneficial effect of metformin. Hum Reprod. 2006;21(6):1426–31.