Journal of Pioneering Medical Sciences
Received: December 29, 2025 | Accepted: March 11, 2026 | Published: May 05, 2026
Volume 15, Issue 04, Pages 42-48
DOI https://doi.org/10.47310/jpms2026150407

The Possible Correlation of Adipokine (Vaspin and Apelin) Serum Levels with Insulin Resistance in a Sample of Iraqi Women with Polycystic Ovary Syndrome

Zahraa Mohammed Ali[1], Mohanad Faris Raheem[2], Najwan Kaisar Fakree[3], Shahad Sabah Khalid[4*] and Mohammed A. Abd[5]
[1,3]Department of Clinical Laboratory Sciences, College of Pharmacy, Baghdad University, Iraq
[2]College of Pharmacy, Department of Clinical Chemistry, AL-Bayan University, Baghdad, Iraq
[4,5]College/Department of Pharmacy, Al-Nukhba University, Baghdad, Iraq

Author Designation: [1,3]Lecturer, [2,4,5]Assistant Lecturer

*Corresponding author: Shahad Sabah Khalid (e-mail: s.sabahph@alnukhba.edu.iq).

Abstract **Background**: Polycystic ovarian syndrome (PCOS), a complex endocrine condition, is often connected to obesity and insulin resistance. Adipokines like vaspin and apelin may contribute to PCOS-related metabolic abnormalities, although studies from Middle Eastern populations are limited. This research compared serum vaspin and apelin levels to insulin resistance in Iraqi women with PCOS. **Methods**: The present cross-sectional research involved 48 women, comprising 30 obese patients with PCOS and 18 age-matched healthy controls. Fasting blood samples were analysed for glucose, insulin, vaspin and apelin using ELISA. Insulin resistance was evaluated using HOMA-IR. Statistical analyses included t-tests, Pearson correlation and ROC analysis. **Results**: Women with PCOS had substantially elevated serum concentrations of vaspin, apelin, glucose, insulin and HOMA-IR ($p<0.001$). A strong correlation was observed between vaspin and apelin ($r = 0.949$, $p<0.001$). Vaspin had a moderate correlation with HOMA-IR ($r = 0.453$, $p<0.001$), however apelin did not show a similar connection. Vaspin had the highest diagnostic accuracy (AUC = 0.992), followed by HOMA-IR (AUC = 0.826) and apelin (AUC = 0.819). **Conclusion**: The elevated concentrations of vaspin and apelin in obese women with PCOS suggest their potential use as biomarkers for detecting and monitoring metabolic dysfunction in this population.

Key Words Polycystic Ovary Syndrome, Vaspin, Apelin, ROC analysis, Correlation

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age; however, its aetiology remains unidentified [1]. Obesity, insulin resistance and cardiovascular diseases (CVD) are among the metabolic alterations and manifestations linked to PCOS, women with PCOS have changes in intraovarian and systemic metabolite concentrations; the dysfunction of adipose tissue is crucial in the aetiology of PCOS [2]. Metabolic stress impairs adipose tissue development, resulting in adipocyte enlargement and the production of stress signals. Women with PCOS may have metabolic issues due to dysfunctional adipose tissue, resulting from hormonal imbalances, elevated LH levels and increased androgenic characteristics [3]. Women with PCOS are susceptible to the buildup of abdominal or visceral fat, alongside overall obesity, insulin resistance and adverse metabolic profiles are associated with these depots [4]. Adipose tissue releases physiologically active peptides known as adipokines, which are crucial for metabolism and energy management. Among adipokines, vaspin and apelin are notable [5]. Disrupted adipokine production influences metabolism and sex steroid release, possibly impacting the pathogenesis of PCOS [6]. Numerous research has investigated adipokines to ascertain their significance in the aetiology of PCOS; however, no specific biomarker has been identified as a direct causative factor for the disorder. Abnormal adipokine production and insulin resistance (IR) have been shown to be associated with obesity, with IR potentially serving as a link between adipokines and polycystic ovaries [7].

Vaspin is a member of the serine protease inhibitor family and is released by visceral and subcutaneous adipose tissues. Vaspin interacts to a 78-kDa glucose-regulated protein (GRP78) on the cell membrane. The findings indicate a strong correlation between lipid metabolism and

insulin resistance. Vaspin is significantly expressed in the human ovary. It facilitates the synthesis of hormones, proliferation and survival of granulosa cells via the GRP78 receptor, contingent upon its concentration ($p<0.0001$) [8]. Multiple studies indicate that individuals with PCOS have increased circular vaspin levels, perhaps contributing to the insulin resistance mechanism [9, 10]. Prior research identified a correlation between blood vaspin levels and both BMI and the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) across different forms of PCOS [11]. Individuals exhibiting the "classical" phenotype (PCOS diagnosed according to all three criteria) had the greatest concentrations of vaspin in their bloodstream, indicating a correlation between vaspin levels and the severity of PCOS [7]. Apelin, a concise protein of 77 amino acids, may be divided into many active isoforms, including apelin-13 and apelin-17. The G protein-coupled apelin receptor APLNR interacts with all apelin variants. Apelin and APLNR have also been identified in white adipose tissue adipocytes, apelin enhances several physiological processes, including glucose absorption by skeletal muscle and adipocytes, insulin responsiveness, mitochondrial biogenesis and lipid catabolism [12]. It also safeguards against insulin resistance, glucose intolerance, obesity and hypertension and has been shown to possess antifibrotic characteristics [13]. Studies have shown that apelin is involved in tissue fibrosis and inflammation. Obese individuals and those with type 1 or type 2 diabetes have elevated serum apelin concentrations, recent research indicates that the apelin/APJ system governs several physiological and pathological processes and is associated with multiple ailments, including malignancies, aging, eclampsia, hearing loss, metabolic disorders, neurological diseases and ischemia-reperfusion damage [14]. Apelin exerts vasodilatory effects through endothelial nitric oxide pathways, thereby maintaining vascular integrity and promoting glucose uptake; impairment of this mechanism may contribute to insulin resistance pathogenesis via endothelial dysfunction. Vaspin, conversely, is associated with obesity, vascular inflammation and insulin resistance, though its precise mechanistic role remains under investigation [15,16].

There have been studies that have shown links between vaspin or apelin levels and metabolic problems in PCOS, although the findings are not always the same, particularly when looking at different ethnic and geographic groups. There isn't much proof that these links exist in Middle Eastern groups, especially among Iraqi women, who may have different genetic and lifestyle-related risk factors. This study intends to look at how serum vaspin and apelin levels are related to insulin resistance in a group of Iraqi women who have just been diagnosed with PCOS. The goal of this study is to learn more about metabolic problems in PCOS in this population that doesn't get enough attention by looking into how these adipokines may be used to diagnose them.

METHODS

Study Design

There were 48 women in this study, all between the ages of 18 and 40. It was a cross-sectional observational study. The study included two groups: 30 women who had just been diagnosed with PCOS by a specialist doctor and 18 women who were supposedly healthy and made up the control group. All participants had to fast for 12 hours before their samples were taken to make sure that the metabolic tests were the same for everyone. The control group was the same age and came from the same community as the PCOS group to make sure they were identical.

Study Setting

The research was conducted at The Higher Institute for the Diagnosis of Infertility and Assisted Reproduction Techniques, a specialized academic and clinical institution. The study took place between October 1, 2023 and April 1, 2024. The institution provided a standard clinical environment that was good for the consistent evaluation of metabolic and endocrine variables in women of childbearing age. All of the clinical procedures, data collection and lab tests were done in compliance with the rules and moral standards of the institution.

Requirements for Inclusion

Participants could be included if they satisfied all of the following requirements:

- Women between the ages of 18 and 40
- They have to fast for at least 12 hours before taking the sample
- A specialist physician validated the diagnosis of polycystic ovarian syndrome (PCOS) based on accepted diagnostic criteria
- Were considered obese if their body mass index (BMI) was 30 kg/m² or above. Only obese women were included to magnify the contrast in metabolic dysfunction and improve signal detection of adipokine differences

Reasons for Exclusion

The research did not include anyone who satisfied any of the following criteria:

- Having renal problems, cancer or long-term autoimmune conditions.
- At the time of data collection, there was a history of pregnancy
- Taking any medicines that are known to change metabolic or hormonal state in the last several weeks, such as:
    - Insulin or metformin
    - Anticonvulsants
    - Corticosteroids
    - Any kind of treatment containing hormones

Sample Size

The required sample size for this observational study was estimated based on the ability to detect a statistically significant difference in the mean serum vaspin levels between

women diagnosed with polycystic ovary syndrome (PCOS) and healthy control subjects. A two-sided, unpaired Student's t-test was chosen as the appropriate statistical test to compare continuous outcomes between the two independent groups. The sample size calculation was based on the following standard formula for comparing two independent means [17]:

$$n = (2\times(Z1-\alpha/2+Z1-\beta)2\times\sigma2) \div \delta^2$$

n = required sample size per group, α = type I error rate (set at 0.05 for a two-tailed test, β = type II error rate (set at 0.20 to achieve 80% power), $Z_{1-}\alpha/_2 = 1.96$ for 95% confidence, $Z_{1-\beta} =$ 0.84 for 80% power, σ = estimated pooled standard deviation of serum vaspin levels, δ = expected difference in mean vaspin levels between groups supported by similar findings in the literature [18], the following parameters were used: Mean serum vaspin level in PCOS patients: 512.73 pg/mL, Mean serum vaspin level in controls: 124.66 pg/mL, Pooled standard deviation (σ) ≈ 147.29 pg/mL, Expected effect size (δ) = 388.07 pg/mL . Therefore, the minimum required sample size per group was approximately 3 participants to detect a large difference in serum vaspin levels with 80% power at a 5% significance level. However, to enhance the robustness and generalizability of the findings, the actual study included a total of 48 participants (30 obese women with PCOS and 18 healthy controls). This larger sample size allowed for more accurate estimation of associations, improved external validity and accommodated potential data variability or dropout.

Sample Collection and Biochemical Analysis

A total of 10 mL of venous blood was collected from both healthy controls and PCOS participants. Samples were divided into two groups: the first was used for glucose determination, collected in specialized tubes, allowed to coagulate and subsequently centrifuged to obtain serum. The second group was left to coagulate at ambient temperature for one hour, then centrifuged at 1000×g for 20 minutes at 2-8 °C. The resulting supernatant was aliquoted into two portions and stored at -80 °C until analysis. Serum concentrations of insulin, vaspin and apelin were quantified using a commercially available Sandwich-ELISA kit (Elabscience®, USA). Serum glucose levels were determined by the Trinder enzymatic colorimetric method, based on the formation of a quinonimine chromogen, as summarized in Table 1. The Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) was utilized to determine insulin sensitivity or resistance, employing fasting serum glucose and insulin levels, according to the following formula:

$$\text{HOMA-IR} = \text{Fasting Glucose (mmol/ml)} \times \text{Fasting Insulin (µU/ml)} \div 22.5$$

the standardizing range is below 2.5 and elevated levels were deemed symptomatic of insulin resistance [19]. The Body Mass Index (BMI) was computed with the accompanying formula:

$$\text{BMI (kg/m}^2\text{)} = \text{Weight} \div \text{Height}^2$$

A value of ≥30 kg/m² were categorized as obese [20].

Table 1: Summary of reagent and kits used in the study

Chemicals	Provider	Cat. No.
Glucose	LINEAR Chemical (Spain)	NA
Insulin	Elabscience (USA)	E-UNEL-H0101
Apelin	Elabscience (USA)	E-EL-H0456
Vaspin	Elabscience (USA)	E-EL-H1762

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, NY: IBM Corp (ID: SCR_016479) version 27. The Kolmogorov-Smirnov test was used to determine whether the data had a normal distribution. The mean±standard deviation (SD) represents the presentation of descriptive statistics. The unpaired t-test was used to compare the outcomes of normally distributed variables between patients and controls. Pearson's chi-square test was used for categorical variables, while Pearson's correlation test was utilized to assess the relationship between parameters and outcomes. The area under the curve (AUC), optimal cut-off value, specificity and sensitivity were assessed using a receiver operating characteristic (ROC) curve, p value ≤0.05 was considered statistically significant.

RESULTS

There were 48 women in the research, 30 of whom had PCOS and 18 of whom were healthy controls. Table 2 shows a summary of the differences in their baseline anthropometric features. The two groups were not significantly different in age, weight, height or body mass index (BMI). The average age of the PCOS group was 29±5.31 years, whereas the average age of the control group was 31±7.89 years (p = 0.456). In the same approach, there were no significant changes in mean weight (81.73±11.92 kg vs. 77.94±10.22 kg; p = 0.268) or mean height (159.83±5.43 cm vs. 161.22±7.31 cm; p = 0.456). The average BMI of the PCOS group (32.07±6.74 kg/m²) was a little higher than that of the control group (30.07±4.31 kg/m²), although this difference was not statistically significant (p = 0.161).

The study found a significant elevation in fasting glucose, insulin and HOMA-IR serum levels in females with PCOS when compared with a control group with a P-value of<0.05. The levels of vaspin and apelin in the blood were significantly higher in women with PCOS than those in the control group (P-value = 0.001 for apelin and 0.001 for vaspin). The Mean±SD apelin levels in the patients were 486.501±251.984 and 240.894±168.779 for the control group. while for vaspin serum level represented as Mean±SD were 512.73±197.851(pg/ml) for the patients' group and 124.657±70.008 (pg/ml) for the control, as shown in Figure 1.

A strong correlation was observed between serum concentrations of vaspin and apelin (r = 0.949, p<0.001). HOMA-IR exhibited no association with blood apelin levels (p = 0.212), although had a moderate positive correlation with serum vaspin levels (r = 0.453, p<0.001). The investigation revealed no correlation between BMI and vaspin or apelin serum levels, with p-values of 0.110 and 0.103, respectively, as shown in Table 3.

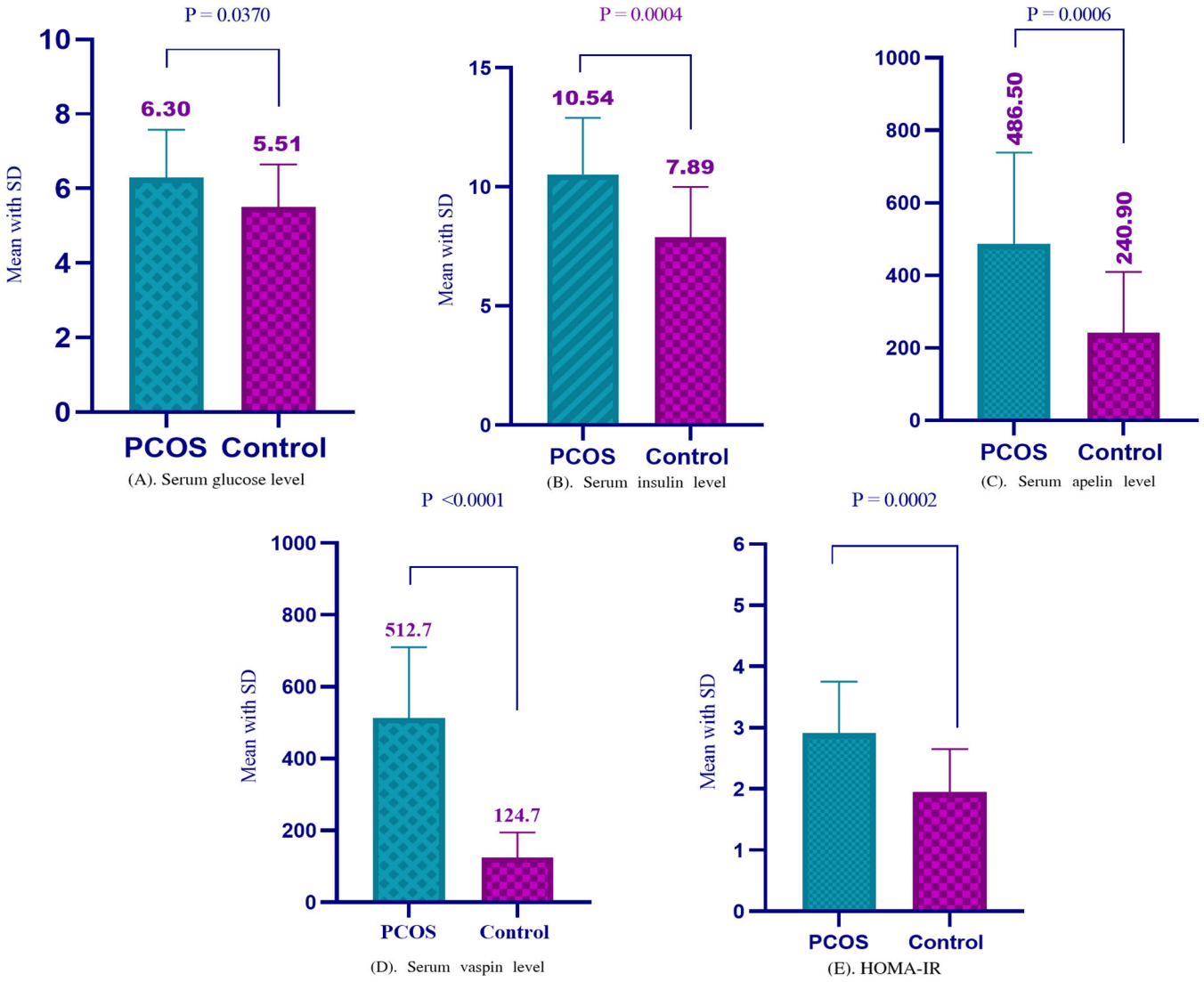

Figure 1 (A-E): Serum biochemical parameters in women with PCOS compared to healthy controls. (A) Fasting glucose (mmol/L), (B) insulin (μIU/mL), (C) apelin (pg/mL), (D) vaspin (pg/mL), (E) HOMA-IR. Data presented as Mean±SD. p<0.05 vs. control

Table 2: Baseline socio-demographic and anthropometric characteristics of women with PCOS and healthy controls

Parameter	Patients (n = 30)	Control (n = 30)	p value
Age (years)	29±5.305	31 ±7.89	0.456
Weight (Kg)	81.73 ±11.92	77.94±10.22	0.268
Height (cm)	159.83±5.43	161.22±7.313	0.456
BMI (kg/m^2)	32.067±30.068	30.068±4.31	0.161

Data expressed as mean±SD, SD: standard deviation, N: number, p-value<0.05 is significant

Vaspin exhibited an AUC of 0.992, indicating its efficacy in diagnosing PCOS in women, with a cut-off value of 228.95 pg/ml and sensitivity and specificity of 96.7% and 83.5%, respectively. Apelin had an AUC of 0.819, indicating its efficacy in diagnosing PCOS in women, with a cut-off value of 248.707 pg/ml and sensitivity and specificity of 80% and 88%, respectively (Table 4 and Figure 2).

DISCUSSION

The present research revealed that the serum vaspin levels of women with PCOS were significantly higher than those of the control group. This was consistent with the results of Mehrabani *et al.* (2021), who conducted a systematic review and meta-analysis of 88 studies. Their findings indicated that women with PCOS exhibited significantly elevated serum vaspin levels [18]. Previous research has shown that glucose is responsible for the substantial increases in vaspin mRNA and protein expression in adipose tissue among PCOS patients, which corroborate these findings. Nevertheless, research has indicated that metformin therapy reduces the levels of vaspin plasma in patients with PCOS [21]. Vaspin expression is intimately linked to lipid metabolism and IR. Elevated vaspin levels in women with PCOS have been demonstrated in numerous studies to contribute to IR [22].

The function of Apelin in the regulation of glucose homeostasis has been suggested and it has been associated with insulin resistance and obesity. Insulin stimulates apelin secretion, while apelin stimulates glucose utilization and inhibits insulin secretion [23-25].

Table 3: Pearson's correlation coefficients (r) between serum apelin, vaspin, HOMA-IR and BMI in women with PCOS

Parameter	Serum apelin level (pg/ml)		Serum vaspin level (pg/ml)	
	r	p value	r	P value
BMI (kg/m²)	0.238	0.103	0.234	0.110
Serum apelin level (pg/ml)	-	-	0.949	<0.001***
Serum vaspin level (pg/ml)	0.949	<0.001*	-	-
HOMA-IR	0.183	0.212	0.453	0.001*

r: Correlation Coefficient, BMI: Body mass index, HOMA-IR: Homeostatic model assessment for insulin resistance, *p<0.05; **p<0.01; ***p<0.001

Table 4: Receiver operating characteristic (ROC) analysis of vaspin, apelin and HOMA-IR in differentiating women with PCOS from healthy controls

Parameter	AUC	P-value	Optimal cut-off point	Sensitivity	Specificity
Serum vaspin level (pg/ml)	0.992	0.0001***	228.95	96.7%	83.5%
Serum apelin level (pg/ml)	0.819	0.0001***	248.707	80%	88%
HOMA-IR	0.826	0.0001***	2.011	83.3%	82.2%

AUC: Area under the curve *p<0.05; **p<0.01; ***p<0.001: Significant, HOMA-IR: Homeostatic model assessment for insulin resistance

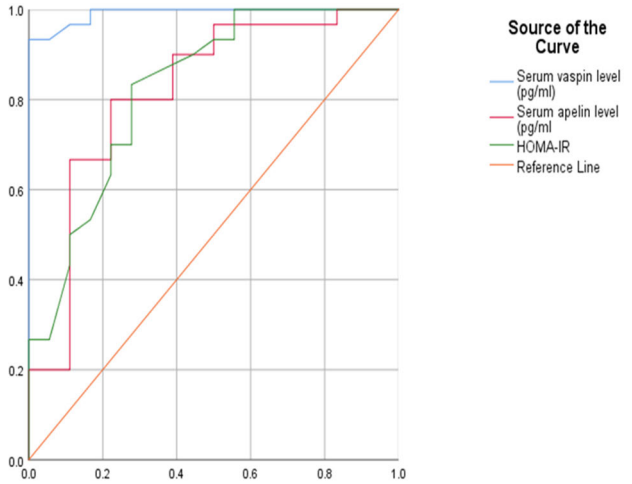

Figure 2: Receiver operating characteristic (ROC) curves for vaspin, apelin and HOMA-IR in discriminating women with PCOS from controls. The curves are color-coded (blue = vaspin, red = apelin, green = HOMA-IR). X-axis = 1 - specificity, Y-axis = sensitivity. The area under the curve (AUC) with 95% confidence intervals is displayed for each marker

The apelin system is a feature of the mammalian ovary, as has been proven. The expression of apelin and APNR in granulosa cells and oocytes was significantly increased as the size of the ovarian follicle increased. Research has shown that the expression of APLNR in granulosa cells is elevated by progesterone. The results of the current study, as illustrated in Table 3, demonstrated a substantial increase in serum apelin levels in the patient group compared to the control group. This finding is consistent with prior research indicating that plasma apelin concentrations are elevated in PCOS patients compared to healthy controls [26].

The serum levels of apelin were substantially higher in the obese and non-obese PCOS groups than in the control group, according to a study conducted in Egypt. Statistically significant positive relationships were observed between Apelin and BMI, as well as HOMA-IR, in the PCOS groups. Despite the fact that all of the patients in this study were obese, the results of this study did not reveal a significant correlation between vaspin or apelin and BMI. However, there was a moderate positive correlation between vaspin and HOMA-IR; but not apelin there are possible explanations for this observation. Theory 1 Apelin has several isoforms (e.g., apelin-13, apelin-36) with different biological activity and ELISA kits used for measurement may recognize all isoforms together and thereby obscure any isoform-specific associations with insulin resistance [27]. Second, circulating apelin concentrations are very stable but probably influenced by obesity, inflammation, vascular burden stress and renal clearance modifying the direct correlations with indices of insulin sensitivity [15]. Third, apelin has central metabolic effects (stimulating glucose uptake through AMPK and Akt signalling) and vascular effects (increasing endothelial nitric oxide bioavailability), raising the possibility that its role in insulin sensitivity may vary depending on context and reflective of endothelium health [28]. Finally, differences on other studies findings may simply reflect differences in population characteristics (age, sex, BMI, ethnicity), sample size and comorbidities which may attenuate or hide the true relationship [29]. These considerations emphasize the necessity of the isoform-specific assays, larger populations and stratification data in future studies to delineate the role of apelin in insulin resistance. The levels of apelin in follicular fluid or apelin expression in granulosa cells were significantly higher in obese women than in normal-weight women and they were strongly correlated with BMI [30].

The number of follicles is associated with apelin levels in follicular fluid and its expression in granulosa cells, as indicated by a distinct study. The scientists made similar noteworthy discoveries with APJ, specifically that the expression of this receptor was more prevalent in women with PCOS and the obese group [31]. A meta-analysis of 81 studies revealed that there were no statistically significant differences in apelin levels between non-obese PCOS relatives and non-obese healthy controls [32].

In addition to the strong positive correlation (r = 0.949, p<0.00) between the serum levels of these two markers in the patient group (Table 4), the role of vaspin and apelin in PCOS was evident from the significant increases in both vaspin and apelin levels in the patient group compared to those in the control group. The exceptionally high correlation between vaspin and apelin (r = 0.949) likely reflects their coproduction in metabolically stressed adipose tissue and shared regulation

by obesity-linked inflammation and insulin signalling disturbances—suggesting parallel, possibly redundant roles that warrant cautious biomarker interpretation and targeted mechanistic exploration [33]. These markers are significant markers that aid in the assessment and follow-up of PCOS-affected women. Additionally, the calculated AUCs for apelin and vaspin were 0.819 and 0.992, respectively, as illustrated in Table 5. This underscores the importance of these two markers as ideal PCOS indicators, as they are both specific and sensitive. apelin has a sensitivity of 87%, while vaspin has a specificity of 72%. Variations in age, ethnicity, study design, genetic attributes and evaluation methodologies could account for the divergent results observed in published research [24].

This study has several limitations first it was conducted at a single academic institution in Iraq, which might make it hard to apply the findings to other groups with different ethnic, healthcare and environmental backgrounds. The research only included 48 patients (30 with PCOS and 18 without), therefore it may not have been able to find small variations or connections, especially when looking at subgroups (such by adiposity or HOMA-IR levels). Because the research was observational and cross-sectional, it is not possible to say whether higher levels of adipokines cause insulin resistance or the development of PCOS. Not measuring important reproductive hormones including LH, FSH, oestradiol and androgens make it hard to understand how hormones interact with apelin and vaspin. We did not examine at any inflammatory biomarkers (such CRP, IL-6 or TNF-α) because we intended to find out if they may have any impacts that might mess up the results. This is because vaspin and apelin are involved in inflammatory pathways. It should be acknowledged that commercially available ELISA kits may detect multiple apelin isoforms, such as apelin-13 and apelin-36, which differ in their biological activity and stability. This heterogeneity could have influenced the measured serum concentrations and potentially affected the interpretation of associations with insulin resistance. This study exclusively enrolled obese women with PCOS (BMI ≥30 kg/m²), thereby excluding the normal-weight PCOS phenotype. Since lean women with PCOS may present distinct metabolic and hormonal profiles compared to their obese counterparts, the findings may not fully capture the heterogeneity of the syndrome, which limits the generalizability of our results. We didn't assess lifestyle variables like stress levels, eating habits and exercise, even though these might affect both insulin sensitivity and adipokine secretion.

CONCLUSIONS

Due to the fact that both vaspin and apelin exhibited a considerable increase in women who were diagnosed with PCOS and that there was a strong association between the levels, these two markers may be considered to be part of the indicators that assisted in the diagnosis and monitoring of women who had PCOS. Their respective roles in this disease are further strengthened by the increased sensitivity and specificity of each of them.

Ethical Statement

Ethical authorization was obtained from the Research Ethics Committee of the University of Baghdad, College of Pharmacy, on September 1, 2023 (Approval No. RECAUCP19203K). Informed consent was obtained from all participants, anonymity was preserved and data were analysed individually. The study fully complied with the principles of the Declaration of Helsinki.

REFERENCES

[1] Opatowski, M. *et al.* "Polycystic ovary syndrome and the risk of premenstrual disorders: A nationwide register-based study in Sweden." *Depression and Anxiety*, vol. 2025, no. 1, 2025, article 8226088. https://doi.org/10.1155/da/8226088.

[2] Senthilkumar, H. and M. Arumugam. "Gut microbiota: A hidden player in polycystic ovary syndrome." *Journal of Translational Medicine*, vol. 23, no. 1, 2025. https://doi.org/10.1155/da/8226088.

[3] Zhang, S. *et al.* "New perspectives on polycystic ovary syndrome: Hypothalamic-sympathetic-adipose tissue interaction." *Journal of Ovarian Research*, vol. 18, no. 1, 2025, article 145. https://doi.org/10.1186/s13048-025-01724-0.

[4] Li, S. *et al.* "α-Linolenic acid-rich flaxseed oil improves polycystic ovary syndrome via regulating lipid metabolism by GPR120-cAMP pathway and restoring gut microecology." *Molecular Nutrition & Food Research*, 2025, article e70136. https://doi.org/10.1002/mnfr.70136.

[5] Martins, F.F. *et al.* "Obesity, white adipose tissue and adipokines signaling in male reproduction." *Molecular Nutrition & Food Research*, vol. 69, no. 10, 2025, article e70054. https://doi.org/10.1002/mnfr.70054.

[6] Dobre, M.-Z. *et al.* "Lipid hormones at the intersection of metabolic imbalances and endocrine disorders." *Current Issues in Molecular Biology*, vol. 47, no. 7, 2025, article 565. https://doi.org/10.3390/cimb47070565.

[7] Abed, W.T. *et al.* "Estimating of the levels of some biochemical variables, adipokines and cytokines in women with polycystic ovarian syndrome." *Journal of Natural Science, Biology and Medicine*, vol. 16, no. 1, 2025, article 91. https://doi.org/10.4103/jnsbm.JNSBM_16_1_10.

[8] Kurowska, P. *et al.* "New aspect on the regulation of in vitro oocyte maturation: Role of obesity, neuropeptides and adipokines." *Journal of Assisted Reproduction and Genetics*, vol. 42, no. 3, 2025, pp. 737-752. https://doi.org/10.1007/s10815-024-03345-w.

[9] Rodríguez, Y.M. *et al.* "Breast cancer shares many epidemiological, lifestyle and local hormonal and metabolic underpinnings with endometrial and ovarian cancer: A narrative review." *Translational Breast Cancer Research*, vol. 6, 2025, article 8. https://doi.org/10.21037/tbcr-24-39.

[10] Pich, K. *et al.* "In vitro effect of omentin-1 on level of other adipokines in granulosa cells from ovaries of Large White and Meishan pigs." *Animal Reproduction Science*, vol. 274, 2025. https://doi.org/10.1016/j.anireprosci.2025.107783.

[11] Mahabamunuge, J. *et al.* "The molecular basis of polycystic ovary syndrome and its cardiometabolic correlates: Exploring the intersection and its clinical implications—A narrative review." *Biomedicines*, vol. 13, no. 3, 2025, article 709. https://doi.org/10.3390/biomedicines13030709.

[12] Yue, Y. *et al.* "Structural insights into the regulation of monomeric and dimeric apelin receptor." *Nature Communications*, vol. 16, no. 1, 2025, article 310. https://doi.org/10.1038/s41467-024-55555-6.

[13] Li, X. and S. Qu. "Novel insights into the central protective role of ACE2 in diabetic cardiomyopathy: From underlying signaling pathways to therapeutic perspectives." *Molecular and Cellular Biochemistry*, vol. 480, no. 6, 2025, pp. 3535-3551. https://doi.org/10.1007/s11010-024-05196-6.

[14] Huang, M. *et al.* "Apelin/APJ increased renal blood flow through endothelial BKCa channel induced p-eNOS and ET-1 in diabetic conditions." *Peptides*, vol. 183, 2025, article 171333. https://doi.org/10.1016/j.peptides.2024.171333.

[15] Yin, C. *et al.* "The role of the adipocytokines vaspin and visfatin in vascular endothelial function and insulin resistance in obese children." *BMC Endocrine Disorders*, vol. 19, no. 1, 2019, article 127. https://doi.org/10.1186/s12902-019-0452-6.

[16] Helker, C.S.M. *et al.* "Apelin signaling drives vascular endothelial cells toward a pro-angiogenic state." *eLife*, vol. 9, 2020, article e55589. https://doi.org/10.7554/eLife.55589.

[17] Charan, J. and T. Biswas. "How to calculate sample size for different study designs in medical research?" *Indian Journal of Psychological Medicine*, vol. 35, no. 2, 2013, pp. 121-126. https://doi.org/10.4103/0253-7176.116232.

[18] Mehrabani, S. *et al.* "Blood circulating levels of adipokines in polycystic ovary syndrome patients: A systematic review and meta-analysis." *Reproductive Sciences*, vol. 28, no. 11, 2021, pp. 3032-3050. https://doi.org/10.1007/s43032-021-00709-w.

[19] Miksza, U. *et al.* "The BDNF protein is associated with glucose homeostasis and food intake in carriers of common BDNF gene variants." *The Journal of Clinical Endocrinology & Metabolism*, vol. 110, no. 2, 2025, pp. e487-e496. https://doi.org/10.1210/clinem/dgae165.

[20] Gümüşdağ, H. *et al.* "Investigation of cardiovascular responses to aerobic exercise in obese university students." *Diabetes & Obesity International Journal*, vol. 10, no. 1, 2025. https://doi.org/10.23880/doij-16000296.

[21] Tan, B.K. *et al.* "Metformin decreases the adipokine vaspin in overweight women with polycystic ovary syndrome concomitant with improvement in insulin sensitivity and a decrease in insulin resistance." *Diabetes*, vol. 57, no. 6, 2008, pp. 1501-1507. https://doi.org/10.2337/db08-0127.

[22] Chen, P. *et al.* "Progress of adipokines in the female reproductive system: A focus on polycystic ovary syndrome." *Frontiers in Endocrinology*, vol. 13, 2022, article 881684. https://doi.org/10.1155/2018/9170480.

[23] Schüler-Toprak, S. *et al.* "The complex roles of adipokines in polycystic ovary syndrome and endometriosis." *Biomedicines*, vol. 10, no. 10, 2022, article 2503. https://doi.org/10.3390/biomedicines10102503.

[24] Dravecká, I. *et al.* "Is apelin a new biomarker in patients with polycystic ovary syndrome?" *Physiological Research*, vol. 70, Suppl 4, 2021, pp. S635-S641. https://doi.org/10.33549/physiolres.934708.

[25] Kurowska, P. *et al.* "Apelin in reproductive physiology and pathology of different species: A critical review." *International Journal of Endocrinology*, vol. 2018, no. 1, 2018, article 9170480. https://doi.org/10.1155/2018/9170480.

[26] Javn, S.B. *et al.* "Polycystic ovarian syndrome-associated cardiovascular complications: An overview of the association between the biochemical markers and potential strategies for their prevention and elimination." *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, vol. 11, 2017, pp. S841-S851. https://doi.org/10.1016/j.dsx.2017.07.004.

[27] Chapman, F.A. *et al.* "The therapeutic potential of apelin in kidney disease." *Nature Reviews Nephrology*, vol. 17, no. 12, 2021, pp. 840-853. https://doi.org/10.1038/s41581-021-00461-z.

[28] Lakin, R. *et al.* "Cardiomyocyte and endothelial cells play distinct roles in the tumour necrosis factor (TNF)-dependent atrial responses and increased atrial fibrillation vulnerability induced by endurance exercise training in mice." *Cardiovascular Research*, vol. 119, no. 16, 2023, pp. 2607-2622. https://doi.org/10.3389/fphys.2019.00010.

[29] Wingelaar, T.T. *et al.* "Pulmonary oxygen toxicity in navy divers: A crossover study using exhaled breath analysis after a one-hour air or oxygen dive at nine meters of sea water." *Frontiers in Physiology*, vol. 10, 2019, article 10. https://doi.org/10.3389/fphys.2019.00010.

[30] Bongrani, A. *et al.* "Ovarian expression of adipokines in polycystic ovary syndrome: A role for chemerin, omentin and apelin in follicular growth arrest and ovulatory dysfunction?" *International Journal of Molecular Sciences*, vol. 20, no. 15, 2019, article 3778. https://doi.org/10.3390/ijms20153778.

[31] Lin, K. *et al.* "Circulating adipokine levels in nonobese women with polycystic ovary syndrome and in nonobese control women: A systematic review and meta-analysis." *Frontiers in Endocrinology*, vol. 11, 2021, article 537809. https://doi.org/10.3389/fendo.2020.537809.

[32] Aktas, B. *et al.* "Serum levels of vaspin, obestatin and apelin-36 in patients with nonalcoholic fatty liver disease." *Metabolism*, vol. 60, no. 4, 2011, pp. 544-549. https://doi.org/10.1016/j.metabol.2010.05.008.