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SERUM APELIN AND CORIN AS BIOCHEMICAL MARKERS OF POLYCYSTIC OVARY SYNDROME

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Background. *Polycystic ovary syndrome (PCOS) is an endocrine-metabolic disease with reproductive dysfunction, intricate hormonal imbalance, elevated risk of cardiovascular disease and obesity in women of reproductive age. Apelin, an adipokine, and corin, a serine protease which activates natriuretic peptide as a cardiovascular regulator, could be involved in the connection between reproductive endocrine imbalance and cardiometabolic regulation in this condition.* ***Objective.*** *To determine apelin and corin levels in the blood of women with PCOS and to evaluate whether they can be useful biochemical predictors for characterizing the disease and stratifying risks.* ***Methods.*** *The case-control study was conducted on 60 women, comprising 30 patients with PCOS and 30 healthy age- and demographically-matched controls. The levels of serum apelin and corin were evaluated with ELISA, that of hormones, 25-hydroxyvitamin D and B_{12} were analyzed with the help of a Finecare analyser.* ***Results.*** *Much higher apelin and corin levels, increased luteinizing hormone (LH) level and LH/follicle-stimulating hormone ratio, and lower 25-hydroxyvitamin D level in the serum of PCOS patients compared to healthy group were detected.* ***Conclusions.*** *The analysis of ROC curves showed significantly positive relationship between hormonal disturbance and the levels of circulating apelin and corin, indicating their higher PCOS diagnostic accuracy compared to the traditional hormonal markers.*

K e y w o r d s: polycystic ovary syndrome, apelin, corin, luteinizing hormone, 25-hydroxyvitamin D.

Polycystic ovarian syndrome (PCOS) is the most common reproductive endocrinopathy in women of reproductive age, affecting roughly 6–8% of women during the reproductive phase, though the frequency varies depending on the diagnostic criteria [1]. Menstrual irregularities, infertility, hyperandrogenism, and insulin resistance are the hallmarks of PCOS [2]. Furthermore, over 50% of patients have higher waist-to-hip ratios (WHR) and android-type obesity, which are linked to an elevated risk of diabetes mellitus and cardiovascular disease [3, 4].

The heart, brain, kidneys, and lungs are among the organs that contain the recently identified peptide apelin, which has been identified as an endogenous receptor ligand [5, 6]. Recent research has shown that different phases of bovine ovarian follicles express apelin and apelin receptor (APJ) at varying amounts [7].

Corin is a transmembrane serine protease which is highly expressed in cardiomyocytes. Its main physiological activity is the proteolytic conversion of pro-atrial natriuretic peptide (pro-ANP) into the biologically active ANP, which is a major regulator of blood pressure, sodium regulation and fluid balance. Corin plays a role in the natriuretic peptide system, thereby playing a role in vasodilation, natriuresis and cardiovascular functionality. Other than the classical cardiovascular action, there is emerging evidence that natriuretic peptides also play a role in metabolic control, adipocyte life and insulin-sensitivity. Furthermore, in light of the predetermined disruption of metabolism in PCOS, characterized by insulin resistance and adipose tis-

sue dysfunction, corin could be a mechanistic connection between cardiometabolic regulation and reproductive endocrine imbalance [8].

Insulin resistance and obesity have been linked to apelin [9, 10]. This adipokine has been demonstrated to affect the hypothalamo-hypophyseal axis and water intake. Additionally, apelin has been shown to affect the cardiovascular system in terms of angiogenesis, positive inotropy, and hypotension [11]. Additionally, the effects of apelin and the apelinergic system on the development of mammalian ovaries, follicular atresia, and the angiogenesis of thecal tissue have been documented [12].

The extracellular portion of human corin has 19 putative N-linked glycosylation sites [13]. Numerous N-glycans on the corin of humans, rats, and mice have been found in studies using cells treated with tunicamycin and glycosidase digestion. These glycans are essential for zymogen activation and corin cell membrane targeting [14, 15]. Corin has not yet been found to contain any sialic acids or O-glycans [16].

Cleavage at the conserved position Arg801-Ile802 activates the zymogen that is corin. The protease domain undergoes conformational modifications as a result of the cleavage, rendering it catalytically active. Enzymatic activity was not evident in purified single-chain corin. Corin's function was eliminated when Arg801 was substituted with Ala, which stopped corin activation. A disulfide bond holds the protease domain to the remainder of the molecule once the Arg801-Ile802 peptide link is broken. Reducing substances like dithiothreitol and β-mercaptoethanol can break disulfide bonds. This technique is employed to differentiate the active form of corin from its zymogen [16]. The corin activator is expected to be a serine protease that prefers basic residues based on the Arg801-Ile802 activation sequence. The corin activator hasn't been identified yet, though.

Transmembrane serine protease corin is mostly found in the heart. Its main function is to change pro-atrial natriuretic peptide (ANP), a precursor peptide, into its active form. Vasodilation, diuresis, and natriuresis are all stimulated as a result of this conversion [17].

In the uterus during pregnancy, corin has been found to play a crucial role in promoting spiral artery remodeling and trophoblast invasion in order to maintain adequate uteroplacental perfusion [18]. According to these research works, the uterine artery perfusion is elevated in healthy women during the luteal period, which coincides with the implantation phase [19]. It can be concluded that corin may be used to enhance endometrial receptivity and during the implantation period. Nevertheless, the mechanism through which corin can be used as a biomarker of human endometrial receptivity at the implantation stage remains unclear.

The current case study aimed to provide a clear assessment of apelin and corin levels in the blood of women with polycystic ovary syndrome (PCOS) compared with healthy controls. Particularly, the aim of this study was to answer the question of whether these biomarkers play a significant role in hormonal and metabolic changes in PCOS and to evaluate whether they can be useful biochemical predictors for characterizing the disease and stratifying risk.

Materials and Methods

A total of 60 women (30 with PCOS) and 30 healthy control) engaged in this case-control study. The participants were recruited at Imameen Kadhimiya Medical City Educational Hospital, Iraq, and all participants provided written informed consent signed prior to enrolment. The diagnosis of PCOS was established according to the Rotterdam criteria (2003), requiring the presence of at least two of the following three features after exclusion of other etiologies: (1) oligo- or anovulation, (2) clinical and/or biochemical signs of hyperandrogenism, and (3) polycystic ovarian morphology confirmed by ultrasound examination. The inclusion criteria included women aged 18 to 40 years; they had to be of normal menstrual cycles and had to have no signs of clinical hyperandrogenism. Women with oligomenorrheia or hyperandrogenism that could not be explained by PCOS, such as congenital adrenal hyperplasia, hyperprolactinemia, and Cushing syndrome, were excluded, as well as those with diabetes mellitus, hypertension, cardiovascular disease, other chronic comorbidities, or pregnancy. The data (clinical and laboratory) were gathered on the basis of the PCOS cases admitted during the study period, and the controls were chosen by a systematic random sampling. The size of the sample was selected based on the availability of patients and the agreed period of conducting the study. A private laboratory accredited by the Baghdad Health Directorate gave ethical approval. There were standardized conditions in collecting the blood samples. The follicle-stimulating hormone (FSH), luteinizing hormone (LH),

prolactin, total testosterone, thyroid-stimulating hormone (TSH), 25-hydroxyvitamin D (25(OH)D) and vitamin B_{12} levels were analyzed using a finecare analyzer according to the protocol or instructions by the manufacturer using the fluorescence immunochromatographic assay (FIA) technique. The concentration of serum apelin and corin was measured in terms of commercially available enzyme-linked immunosorbent assays (ELISA) kits according to the standardized protocols.

Statistical analysis. Quantitative data were analyzed using SPSS version 26. Results are presented as frequencies and percentages. For normally distributed variables, independent and dependent *t*-tests (two-tailed) were used. For non-normally distributed variables, the Mann-Whitney U test, Wilcoxon test, and Chi-square test were applied. A *P*-value of < 0.05 was considered statistically significant.

Ethical approval. The study was approved by the human ethics committee of Al-Imamain Alkadhimain Medical City (Protocol No 123-12, dated 10/3/2025). Everyone who took part in the study was informed and asked to sign a consent form. The patient was also guaranteed that his information would be kept private.

Results

Age and body mass index (BMI) characteristics of women with PCOS and healthy controls. Table 1 demonstrates the sociodemographic and anthropometric data of the study population. The number of women was 60, with 30 patients diagnosed with PCOS and 30 healthy control women. The average age of women in PCOS group (33.31 ± 7.45 years) was similar to that of the control group (31.40 ± 9.01 years), and there was no significant difference between the groups ($P = 0.324$). On the same note, despite the fact that the mean BMI was higher in the PCOS group than in the controls (32.33 ± 4.71 vs. 25.50 ± 2.86 kg/m^2), the difference was not statistically significant ($P = 0.160$), and thus an acceptable level of demographic and anthropometric similarity between the two groups was achieved.

Biochemical profile of women with polycystic ovary syndrome and healthy controls. Table 2 summarizes the biochemical characteristics of the study groups. The mean serum vitamin B_{12} levels were greater in women with PCOS than in healthy controls (312.3 ± 17.5 vs. 265.0 ± 14.87 pg/ml); thus, this was not a statistically significant difference ($P = 0.304$). Conversely, serum 25-hydroxyvitamin D was significantly less in the PCOS group compared to controls (13.46 ± 2.30 vs. 21.56 ± 2.17 ng/ml; $P < 0.001$). Moreover, the level of random blood sugar (RBS) was significantly higher in PCOS patients than in healthy women (5.91 ± 0.31 vs. 5.18 ± 0.29 mg/dl; $P < 0.001$), which showed the presence of a significant change in the metabolic and vitamin parameters of PCOS.

Anthropometric and hormonal characteristics of the study participants. The comparison of the main hormonal parameters of the women with PCOS and healthy control subjects is presented in Table 3. The serum LH concentration was found to be very high in the PCOS group as compared to controls (7.57 ± 0.79 vs. 5.07 ± 0.42 IU/l; $P < 0.001$). Though

Table 1. Comparison of age and body mass index between study groups

Variable	Groups, (n = 30, mean ± SD)		*P*-value
	PCOS	Control	
Age, years	33.31 ± 7.45	31.40 ± 9.01	0.324
BMI, kg/m^2	32.33 ± 4.71	25.50 ± 2.86	0.160

Table 2. Comparison of serum vitamin B_{12}, vitamin D_3, and random blood sugar levels (mean ± SD)

Variable	Groups		*P*-value
	PCOS	Control	
B_{12}, (pg/ml)	312.3 ± 17.5	265.00 ± 14.87	0.304
25-hydroxyvitamin D, ng/ml	13.46 ± 2.30	21.56 ± 2.17	< 0.001
RBS, mmol/l	5.91 ± 0.31	5.18 ± 0.29	< 0.001

the level of FSH was a little lower among PCOS patients than controls (4.77 ± 0.67 vs. 4.84 ± 0.58 IU/l), the result was not significant *(P* = 0.667). Therefore, the ratio of LH/FSH in the PCOS group compared to controls (1.62 ± 0.27 vs. 1.07 ± 0.18; *P* < 0.001) was significantly higher. Conversely, no statistically significant differences were found between the two groups when it comes to serum testosterone (*P* = 0.144) or prolactin levels (*P* = 0.475). Such results indicate the typical imbalance of gonadotropins seen in PCOS and show similar androgen and prolactin levels in the participants of the study.

Circulating levels of apelin and corin in women with polycystic ovary syndrome and healthy control. Table 4 shows the comparison between the serum apelin and corin levels in women with PCOS and healthy control participants. The levels of apelin in the circulation of the PCOS patients were significantly higher than those of the controls (0.38 ± 0.06 vs. 0.20 ± 0.05; *P* < 0.001). Similarly, there was a significant correlation between serum corin levels and the PCOS group as compared to the control group (1311.33 ± 247.87 vs. 788.17 ± 160.87 pg/ml; *P* < 0.001). Such great differences indicate a possible role of apelin and corin in cardiometabolic and endocrine dysregulation of PCOS.

Correlation analysis between apelin levels and clinical, hormonal, and metabolic parameters. Table 5 presents the correlation analysis between serum apelin concentration and the studied clinical, hormonal, and metabolic parameters. The correlation coefficient (*r*) represents the strength and direction of the linear association, while the *P*-value indicates the statistical significance of this relationship. No significant correlations were observed between apelin and age (*r* = −0.011, *P* = 0.931), FSH (*r* = 0.013, *P* = 0.923), prolactin (*r* = −0.137, *P* = 0.298), or testosterone (*r* = 0.112, *P* = 0.396). In contrast, apelin demonstrated a statistically significant positive correlation with BMI (*r* = 0.531, *P* < 0.001), LH (r = 0784, *P* < 0.001), LH/FSH ratio (*r* = 0.628, *P* < 0.001), RBS (*r* = 0.656, *P* < 0.001), and corin levels (*r* = 0.608, *P* < 0.001). These findings indicate that elevated apelin levels are moderately to strongly associated with markers of adiposity, gonadotropin imbalance, metabolic dysregulation, and natriuretic peptide pathway activity, supporting its potential role as an integrated cardiometabolic–endocrine biomarker in PCOS.

Diagnostic performance of hormonal and novel biomarkers in the study population. Table 6 gives the receiver operating characteristic (ROC) analysis of the diagnostic accuracy of the chosen hormonal and biochemical parameters. LH had a good diagnostic performance with the area under the curve (AUC) of 1.000 (*P* <0.001), while the LH/FSH ratio also had a high discriminative value (AUC = 0.958, *P* < 0.0001). Conversely, the FSH had poor diagnostic ability (AUC = 0.448, *P* = 0.1923), and prolactin had poor and non-significant discriminative power (AUC = 0.422, *P* = 0.0559). It is noteworthy that the novel biomarkers apelin and corin showed excellent

Table 3. Comparison of gonadotropins, androgen levels, and prolactin between PCOS patients and healthy control (mean ± SD)

Parameters	Groups		*P*-value
	PCOS	Control	
LH, IU/l	7.57 ± 0.79	5.07 ± 0.42	< 0.001
FSH, IU/l	4.77 ± 0.67	4.84 ± 0.58	0.667
LH/FSH	1.62 ± 0.27	1.07 ± 0.18	< 0.001
Testo, ng/ml	0.22 ± 0.05	0.20 ± 0.05	0.144
Prolactin, IU/l	16.84 ± 2.86	17.43 ± 3.45	0.475

Table 4. Comparative analysis of novel cardiometabolic biomarkers between study groups

Parameters	Groups		*P*-value
	PCOS	Control	
Apelin, ng/ml	0.38 ± 0.06	0.20 ± 0.05	< 0.001
Corin, pg/ml	1311.33 ± 247.87	788.17 ± 160.87	< 0.001

Table 5. Associations of apelin with anthropometric indices, gonadotropins, metabolic markers, and corin levels

Parameters	*r*	*P*
Age	-0.011-	0.931
BMI	0.531**	0.000
LH	0.784**	0.000
FSH	0.013	0.923
LH/FSH	0.628**	0.000
Prolactin	0.137-	0.298
Testo	0.112	0.396
RBS	0.656**	0.000
Corin	0.608**	0.000

Note. **Correlation is significant at $P < 0.01$

Table 6. Receiver operating characteristic (ROC) curve analysis of hormonal parameters, apelin, and corin

Parameters	AUC	*P*-value
LH	1.000	< 0.001
FSH	0.448	0.1923
LH/FSH	0.958	< 0.001
Prolactin	0.422	0.0559
Apelin	1.000	< 0.001
Corin	0.996	< 0.001

diagnostic results with an AUC of 1.000 and 0.996, respectively (both $P < 0.001$). These results underline the positive diagnostic value of apelin and corin in comparison with the classical hormonal biomarkers.

Discussion

PCOS is recognized as one of the most prevalent endocrine–metabolic disorders affecting women of reproductive age and represents a major public health concern due to its heterogeneous clinical manifestations and long-term metabolic and cardiovascular consequences [20]. The etiology of PCOS is not completely understood, with the underlying pathogenic mechanisms of the disease still needing clarification. There is growing evidence to suggest that dysfunction and dysregulation of adipose tissue and the dysfunction of adipokines and natriuretic peptides-related pathways are critical contributors to the essential metabolic imbalances in PCOS [21]. In the current research, women with PCOS exhibited markedly higher concentrations of apelin and corin compared to healthy controls, alongside higher LH levels, an elevated LH/FSH ratio, and a statistically significant but insignificant increase in BMI and glucose levels. The results suggest that cardiometabolic dysregulation and gonadotropin imbalance are not only comorbid in PCOS, but it may also be biologically related. The positive associations between apelin and BMI, LH, LH/FSH ratio, glucose and corin are strong, and therefore the hypothesis that apelin is involved in the integrated endocrine-metabolic derangements of this syndrome is supported [22].

One of the hypothesized mechanisms, decreased ANP system activity, has also been pointed

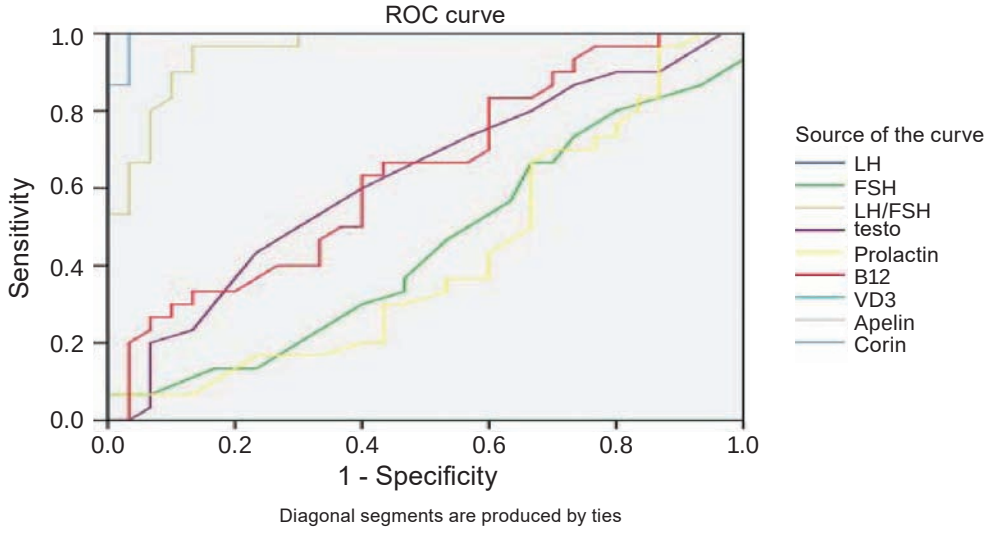

Fig. ROC analyses of apelin and corin and other hormonal assays

out as a cause of metabolic abnormalities of PCOS. Recent discoveries have placed a new player in this system: corin, which is a transmembrane serine protease that activates pro-ANP. Despite the fact that the role of corin has already been thoroughly examined in cardiovascular physiology, its role in the pathogenesis of reproductive endocrinology and PCOS has not been well investigated. The heterogeneous clinical manifestation of PCOS can slow down the process of diagnosis and intervention, hence the need to have effective preclinical biomarkers. Circulating corin, in this regard, can also be a good candidate to utilize as an early risk stratification and disease prediction factor in PCOS [23]. Our results of substantially high levels of circulating corin in PCOS women are consistent with previous reports of the connection between the dysfunction of the natriuretic peptide system and metabolic disease. Although lower ANP in the insulin-resistant state has been characterized, the rise in corin that was found in our cohort could be indicative of activity compensation of the natriuretic peptide pathway to metabolic stress. This is consistent with newer evidence showing that cardiometabolic biomarkers may carry endocrine implications beyond cardiovascular regulation.

Corin is present in membrane-bound and soluble circulating forms, and there is evidence suggesting that soluble corin is as biologically active as its tissue-bound counterpart and plays a role in the processing of natriuretic peptides in the circulation [24]. This biological property can support the hypothesis that increased or decreased levels of corin indicate systemic endocrine and metabolic disruptions in PCOS. In this regard, the current case-control study was modeled to evaluate the possibility of the role of circulating corin as a biomarker that is associated with the pathophysiology of PCOS.

Simultaneously, the apelin-APLN receptor (APLNR) system has become more and more popular as a contributor to the physiology of the ovary. There is expression of apelin and its receptor in ovarian granulosa cells and oocytes and dynamic regulation during the ovarian cycle. Their level of expression decreases with corpus luteum regression and rises with follicular growth, indicating that they are involved in the regulation of folliculogenesis, luteal and angiogenesis [25]. APLNR has been demonstrated to be upregulated by progesterone, demonstrating a bidirectional interaction between luteal hormones and the apelin system [26].

Findings of the past research on the circulating levels of apelin in PCOS have been inconsistent with some studies reporting elevated, lower, or equal levels in comparison to healthy controls [27, 28]. These inconsistencies can be explained by variations in the study design, obesity status, insulin resistance, and metabolic heterogeneity among PCOS populations. However, the mounting body of evidence indicates the role of apelin in PCOS-associated metabolic dysregulation, specifically in the case of insulin resistance, adiposity, and androgen excess [29]. Compared to other reports that indicate a drop in the levels of apelin in obese populations with PCOS, they indicated a considerable rise in circulating apelin concentrations. The difference could be explained by ethnic variations, metabolic phenotype variations, BMI distribution variations, or by assay profiling. Notably, these close associations between apelin and gonadotropin imbalance, as well as glucose in our study, indicate that elevated apelin might be a manifestation of active metabolic-endocrine crosstalk and not merely adiposity.

Mechanistically, it seems that apelin has effects on corpus luteum angiogenesis and activity. Luteal progesterone impairment, which is a characteristic of the luteal phase insufficiency in PCOS, can also be a contributing factor to the impaired APLNR expression, which further worsens ovulatory dysfunction and infertility [30]. In addition to that, the main features of PCOS, a combination of insulin resistance and hyperinsulinemia, can also worsen reproductive failure by impairing the luteal steroidogenesis and angiogenic balance. Though the glucose level in the PCOS group showed to be within the upper range of normoglycemia, the mean value (around 5.9 mmol/l) is close to the upper limit of impaired fasting glucose, as suggested by international clinical guidelines, which state that normal fasting glucose should be less than 5.6 mmol/l. Such a slight increase, even within the normal range for non-diabetic levels, could indicate initial metabolic deregulation and insulin resistance, which are the key elements of PCOS pathophysiology [30]. Although vitamin B_{12} was included in the biochemical assessment due to its known role in metabolic regulation and potential association with insulin resistance, no statistically significant difference was observed between women with PCOS and healthy controls in the present study. Furthermore, vitamin B_{12} did not demonstrate discriminative diagnostic performance in ROC analysis. These findings suggest that, within this specific

cohort, vitamin B_{12} does not appear to function as an independent or sensitive biomarker for PCOS when compared to novel cardiometabolic markers such as apelin and corin. Therefore, while vitamin B_{12} may contribute to broader metabolic assessment, it did not provide additional diagnostic value in distinguishing PCOS cases in this study [31].

Insulin-like growth factor-1 (IGF-1) has also been suspected in ovarian steroidogenesis and follicular maturation in PCOS [31]. High bioactivity of IGF-1 triggered by insulin-induced inhibition of insulin-binding protein-1 (IGFBP-1) has the potential to increase apelin, APLNR gene expression, and trigger estrogen production in granulosa and luteal cells [32]. This adaptive response to ovarian dysfunction in PCOS may be seen in this compensatory increase in the IGF-1-apelin axis [33].

Also, ovarian angiogenesis is crucial to the development of follicles and reproductive health. The vascular endothelial growth factor (VEGF) is significantly increased in PCOS women and plays a role in the formation of cysts and follicular arrest by activating the tyrosine kinase signaling pathways [34]. It was demonstrated that the apelin/APLNR system can occur upstream of VEGF and induce ovarian angiogenesis and structural remodeling. Hyperinsulinemia can also increase VEGF and apelin expression, which strengthens the connection between metabolic regulation and ovarian pathology in PCOS [35].

A number of studies have shown that there are strong relationships between the level of apelin and metabolic indices, such as body mass index, insulin resistance, fasting glucose, triglycerides, and androgen levels [36]. The decreased level of apelin in the circulation has been described specifically in obese PCOS women, which seems to justify its possible use as an indicator of insulin sensitivity. On the other hand, increased expression of apelin in both ovarian tissue and follicular fluid has been reported in PCOS, indicating that there is no relationship between systemic and local apelin activity in the ovaries [37].

It was interesting to note that there is a positive correlation between apelin expression in granulosa cells and follicle number and obesity, and that the APLNR expression is upregulated in PCOS ovaries concomitantly [38]. However, despite the increased activity of local ovarian apelin, certain findings failed to identify any significant relationships between plasma apelin and clinical or biochemical prognosis, which highlights the challenge in apelin regulation and apelin tissue-specific functions in PCOS. Taken together, our results can contribute to the expanding the idea of a non-reproductive cardiometabolic condition of PCOS, which might be associated with adipokine imbalance, alterations in the natriuretic peptide pathway, and endocrine disruption. This research can help advance the current literature, indicating that apelin and corin would be beneficial to use alongside conventional hormonal markers in detecting disease at a very early stage and classifying risks.

Limitations. This study has a number of limitations to be noted. First, the relatively small sample size might make the results less generalizable and less statistically robust. Second, the case–control design does not permit establishing causal relationships between apelin, corin, and pathophysiology of PCOS. Third, the study focused only on selected markers of hormonal, metabolic, and cardiometabolic function, and other markers that could be of relevance have not been assessed. Further, the study was done at one center, limiting the generalizability of the results. Thus, the limitations of the study should be accounted for when interpreting the findings and more studies with larger multicenter patient cohorts should be undertaken to confirm the current results.

Conclusions. Combined, the evidence present suggests a complex contribution of apelin and corin to the endocrine, metabolic and angiogenic disruption of PCOS. The results of the current study contribute to this increasing literature by supporting the possible diagnostic and pathophysiological significance of these biomarkers. Their clinical utility and whether apelin and corin can be used as combined biomarkers to detect the disease at an early stage, stratify the disease, and provide specific therapeutic intervention should be the focus of further large-scale and mechanistic research.

Author contributions. Abbas Mosad Ajeed contributed to study conceptualization, methodology, data collection, laboratory work, and manuscript drafting. Rawnaq J. Kadhim participated in investigation, data analysis, and interpretation of results. Noor Jamil Abbas contributed to methodology, statistical analysis, validation, and data organization. Nesreen Ahmed Nasser supervised the study, contributed to study design, critically revised the manuscript, and approved the final version for publication. All authors read and approved the final manuscript.

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АПЕЛІН ТА КОРІН У СИРОВАТЦІ КРОВІ ЯК БІОХІМІЧНІ МАРКЕРИ СИНДРОМУ ПОЛІКІСТОЗНИХ ЯЄЧНИКІВ

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Вступ. Синдром полікістозних яєчників (PCOS) – це ендокринно-метаболічне захворювання, що супроводжується репродуктивною дисфункцією, гормональним дисбалансом, підвищеним ризиком серцево-судинних захворювань та ожиріння у жінок репродуктивного віку. Апелін, адипокін, і корін, серинова протеаза, яка активує натрійуретичний пептид – регулятор серцево-судинної системи, можуть бути залучені до взаємозв'язку між репродуктивним ендокринним дисбалансом і кардіометаболічною регуляцією за цього стану. **Мета.** Визначити рівні апеліну та коріну в крові жінок із синдромом полікістозних яєчників і оцінити, чи можуть вони бути використані як біохімічні предиктори для характеристики захворювання та стратифікації ризиків. **Методи.** Дослідження типу "випадок-контроль" було проведено за участю 60 жінок, зокрема 30 пацієнток із PCOS та 30 здорових жінок контрольної групи, подібні за віком та демографічними показниками. Рівні апеліну та коріну в сироватці крові оцінювали методом IEA, а рівні гормонів, 25-гідроксивітаміну D та вітаміну B_{12} аналізували за допомогою аналізатора Finecare. **Результати.** У пацієнток із PCOS порівняно зі здоровою групою було виявлено значно вищі рівні апеліну та коріну, підвищений рівень лютеїнізувального гормону (ЛГ) і співвідношення ЛГ/фолікулостимулювального гормону, а також нижчий рівень 25-гідроксивітаміну D у сироватці крові. **Висновки.** Аналіз ROC-кривих показав статистично значущий позитивний зв'язок між гормональними порушеннями та рівнями апеліну та коріну в крові, що свідчить про вищу діагностичну точність цих показників у разі PCOS порівняно з традиційними гормональними маркерами.

Ключові слова: синдром полікістозних яєчників, апелін, корін, лютеїнізувальний гормон, 25-гідроксивітамін D.

References

1. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J *Clin Endocrinol Metab.* 2004; 89(6): 2745-2749.
2. Taylor AE, McCourt B, Martin KA, Anderson EJ, Adams JM, Schoenfeld D, Hall JE. Determinants of abnormal gonadotropin secretion in clinically defined women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 1997; 82(7): 2248-2256.
3. Slowey MJ. Polycystic ovary syndrome: new perspective on an old problem. *South Med J.* 2001; 94(2): 190-196.
4. Wild RA. Obesity, lipids, cardiovascular risk, and androgen excess. *Am J Med*. 1995; 98(1A): 27S-32S.
5. Tatemoto K, Hosoya M, Habata Y, Fujii R, Kakegawa T, Zou MX, Kawamata Y, Fukusumi S, Hinuma S, Kitada C, Kurokawa T, Onda H, Fujino M. Isolation and characterization of a novel endogenous peptide ligand for the human APJ receptor. *Biochem Biophys Res Commun*. 1998; 251(2): 471-476.
6. Ladeiras-Lopes R, Ferreira-Martins J, Leite-Moreira AF. The apelinergic system: the role played in human physiology and pathology and potential therapeutic applications. *Arq Bras Cardiol*. 2008; 90(5): 343-349.
7. Shimizu T, Kosaka N, Murayama C, Tetsuka M, Miyamoto A. Apelin and APJ receptor expression in granulosa and theca cells during different stages of follicular development in the bovine ovary: Involvement of apoptosis and

hormonal regulation. *Anim Reprod Sci*. 2009; 116(1-2): 28-37.
8. Schilffarth S, Antoni B, Schams D, Meyer HH, Berisha B. The expression of apelin and its receptor APJ during different physiological stages in the bovine ovary. *Int J Biol Sci*. 2009; 5(4): 344-350.
9. Boucher J, Masri B, Daviaud D, Gesta S, Guigné C, Mazzucotelli A, Castan-Laurell I, Tack I, Knibiehler B, Carpéné C, Audigier Y, Saulnier-Blache JS, Valet P. Apelin, a newly identified adipokine up-regulated by insulin and obesity. *Endocrinology*. 2005; 146(4): 1764-1771.
10. Heinonen MV, Purhonen AK, Miettinen P, Pääkkönen M, Pirinen E, Alhava E, Akerman K, Herzig KH. Apelin, orexin-A and leptin plasma levels in morbid obesity and effect of gastric banding. *Regul Pept*. 2005; 130(1-2): 7-13.
11. Reaux-Le Goazigo A, Morinville A, Burlet A, Llorens-Cortes C, Beaudet A. Dehydration-induced cross-regulation of apelin and vasopressin immunoreactivity levels in magnocellular hypothalamic neurons. *Endocrinology*. 2004; 145(9): 4392-4400.
12. Ishida J, Hashimoto T, Hashimoto Y, Nishiwaki S, Iguchi T, Harada S, Sugaya T, Matsuzaki H, Yamamoto R, Shiota N, Okunishi H, Kihara M, Umemura S, Sugiyama F, Yagami K, Kasuya Y, Mochizuki N, Fukamizu A. Regulatory roles for APJ, a seven-transmembrane receptor related to angiotensin-type 1 receptor in blood pressure *in vivo*. *J Biol Chem*. 2004; 279(25): 26274-26279.
13. Yan W, Sheng N, Seto M, Morser J, Wu Q. Corin, a mosaic transmembrane serine protease encoded by a novel cDNA from human heart. *J Biol Chem*. 1999; 274(21): 14926-14935.
14. Langenickel TH, Pagel I, Buttgereit J, Tenner K, Lindner M, Dietz R, Willenbrock R, Bader M. Rat corin gene: molecular cloning and reduced expression in experimental heart failure. *Am J Physiol Heart Circ Physiol*. 2004; 287(4): H1516-H1521.
15. Gladysheva IP, King SM, Houng AK. N-glycosylation modulates the cell-surface expression and catalytic activity of corin. *Biochem Biophys Res Commun*. 2008; 373(1): 130-135.
16. Liao X, Wang W, Chen S, Wu Q. Role of glycosylation in corin zymogen activation. *J Biol Chem*. 2007; 282(38): 27728-27735.
17. Zhou Y, Wu Q. Role of corin and atrial natriuretic peptide in preeclampsia. *Placenta*. 2013; 34(2): 89-94.
18. Cui Y, Wang W, Dong N, Lou J, Srinivasan DK, Cheng W, Huang X, Liu M, Fang C, Peng J, Chen S, Wu S, Liu Z, Dong L, Zhou Y, Wu Q. Role of corin in trophoblast invasion and uterine spiral artery remodelling in pregnancy. *Nature*. 2012; 484(7393): 246-250.
19. Check JH, Dietterich C, Lurie D, Nazari A. No evidence of increased uterine vascular impedance with patient ageing following IVF. *Hum Reprod*. 2000; 15(8): 1679-1684.
20. Zhang Y, Chen ZJ, Zhao H. Polycystic ovary syndrome: A metabolic disorder with therapeutic opportunities. *Cell Metab*. 2025; 37(10): 1932-1949.
21. Stener-Victorin E, Teede H, Norman RJ, Legro R, Goodarzi MO, Dokras A, Laven J, Hoeger K, Piltonen TT. Polycystic ovary syndrome. *Nat Rev Dis Primers*. 2024; 10(1): 27.
22. Zhang S, Jiang N, Liu G, Zhang B, Xu H, Xu Y, Qin G, Wang Y, Zhang L, Yang B, Han L. New perspectives on polycystic ovary syndrome: hypothalamic-sympathetic-adipose tissue interaction. *J Ovarian Res*. 2025; 18(1): 145.
23. Li H, Sun S, Guo W, Wang L, Zhang Z, Zhang Y, Zhang C, Liu M, Zhang S, Niu Y, Dong N, Wu Q. Positively charged cytoplasmic residues in corin prevent signal peptidase cleavage and endoplasmic reticulum retention. *Commun Biol*. 2025; 8(1): 89.
24. Shokrollahi B, Zheng HY, Li LY, Tang LP, Ma XY, Lu XR, Duan AQ, Zhang Y, Tan XH, Huang CX, Xu YY, Shang JH. Apelin and Apelin Receptor in Follicular Granulosa Cells of Buffalo Ovaries: Expression and Regulation of Steroidogenesis. *Front Endocrinol (Lausanne)*. 2022; 13: 844360.
25. Mehri K, Hamidian G, Zavvari Oskuye Z, Nayebirad S, Farajdokht F. The role of apelinergic system in metabolism and reproductive system in normal and pathological conditions: an overview. *Front Endocrinol (Lausanne)*. 2023; 14: 1193150.
26. Abdulmuttaleb NA, Oliwi Nasir AA, Alkubaisy SA, Mohsein OA. Investigation of Genetic Variations in APLN and APLNR Genes and Their Potential Role in Cardiovascular Diseases. *Rep Biochem Mol Biol*. 2025; 13(4): 525-539.

27. Gao Y, Xin C, Fan H, Sun X, Wang H. Circulating apelin and chemerin levels in patients with polycystic ovary syndrome: A meta-analysis. *Front Endocrinol (Lausanne).* 2023; 13: 1076951.
28. Ruan X, Li M, Min M, Ju R, Wang H, Xu Z, Luo S, Mueck AO. Plasma visfatin and apelin levels in adolescents with polycystic ovary syndrome. *Gynecol Endocrinol*. 2023; 39(1): 2216807.
29. Mlyczyńska E, Kieżun M, Kurowska P, Dawid M, Pich K, Respekta N, Daudon M, Rytelewska E, Dobrzyń K, Kamińska B, Kamiński T, Smolińska N, Dupont J, Rak A. New Aspects of Corpus Luteum Regulation in Physiological and Pathological Conditions: Involvement of Adipokines and Neuropeptides. *Cells.* 2022; 11(6): 957.
30. Sakban GH, Muhammed TM, Al-Tameemi ZAH, Mohsein OA. Exploring biomarkers, adipokines, and cytokines in patients with colon cancer: a comparative study with healthy controls. *Regul Mech Biosyst*. 2025; 16(3): e25150.
31. Li H, Zhang Y, Liu C, Zhang Y, Yang H, Fu S, Lv H. Association of Insulin-Like Growth Factor-1 With Polycystic Ovarian Syndrome: A Systematic Review and Meta-analysis. *Endocr Pract*. 2023; 29(5): 388-397.
32. Chen C, Jiang X, Ding C, Sun X, Wan L, Wang C. Downregulated lncRNA HOTAIR ameliorates polycystic ovaries syndrome via IGF-1 mediated PI3K/Akt pathway. *Gynecol Endocrinol*. 2023; 39(1): 2227280.
33. Ozen FZ, Kaya-Sezginer E, Kırlangıc OF, Taskomur AT, Aktan F, Kaplan G, Ozgurtas T. Vascular endothelial growth factor (VEGF)-C and its receptors, soluble VEGFR-2 and VEGFR-3, in polycystic ovary syndrome. *Turk J Biochem*. 2024; 49(2): 266-273.
34. Ahmed AW, Abdul-QaderKhuder H, Jasim SAH, Mohsein OA. Hormonal profiles and metabolic changes in women diagnosed with concomitant Hashimoto's thyroiditis and polycystic ovary syndrome via sonography. *Eur J Clin Exp Med*. 2025; 23(3): 596-604.
35. Matta RA, Saedii AA. Cross-Talk between Apelin, Insulin Resistance, Thyroid Hormones, and Cardio-metabolic Risk Factors in Polycystic Ovary Syndrome. *Egypt J Hosp Med*. 2022; 87(1): 1635-1643.
36. Ajeed AM, Naif NH, Farag AH, Mohsein OA. Assessing the impact of sleeve gastrectomy on micronutrient levels and inflammatory markers – a case-control study. *Eur J Clin Exp Med*. 2025; 23(2): 369-377.
37. Chen P, Jia R, Liu Y, Cao M, Zhou L, Zhao Z. Progress of Adipokines in the Female Reproductive System: A Focus on Polycystic Ovary Syndrome. *Front Endocrinol (Lausanne).* 2022; 13: 881684.
38. Abdullah NN, Alameri MA, Muhammed TM, Mohsein OA. Role of Chemerin and Omentin in Predicting Ovulatory Dysfunction in Obese Women With Polycystic Ovary Syndrome (PCOS). *Indones J Med Lab Sci Technol*. 2026; 8(1): 76-83.