Serum Apelin Level and Its Association with Polycystic Ovarian Syndrome: Evaluating Correlations with Obesity in Iraqi Women

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Abstract

Background	One of the most current endocrine conditions influencing women in their fertile age is polycystic ovary syndrome (PCOS). It is a varied condition marked by hyperandrogenism, irregular ovulation, and polycystic ovary morphology, along with abnormalities in metabolism like obesity and insulin resistance. Apelin's function in controlling glucose homeostasis has been investigated, and it has been associated with obesity and insulin resistance. Apelin secretion is stimulated by insulin, whereas insulin secretion is inhibited and glucose utilization is stimulated by Apelin.
Objective	To evaluate the role of Apelin in women with PCOS and its correlation with body mass index (BMI) as an obesity marker .
Methods	Ninety-six adult women were involved in the study, sixty of them were diagnosed with PCOS compared to thirty-six healthy controls as an observational, case-control study. Upon interviewing participants one by one by the researcher, data like BMI were collected as a part of a structured questionnaire, blood samples were obtained. Apelin serum level were measured by enzyme-linked immunosorbent assay (ELISA) analysis using a specialized kit.
Results	The study found a markable increase in Apelin serum levels in women with PCOS group compared with controls with a P value of 0.001, and the descriptive statistic was mean±SD was 486.5±251.98 (pg/ml) while for control was 240.89±168.78 (pg/ml). Apelin had an area under curve of 0.819, which made it good as a diagnostic marker for PCOS in female patients, with a cut-off value of 206.32 pg/ml and sensitivity and specificity of 87% and 61% respectively.
Conclusion	Apelin may represent a BMI-independent marker of PCOS, underscoring its potential relevance in disease pathophysiology.
Keywords	Apelin, PCOS, BMI
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List of abbreviations: BMI = Body Mass Index, PCOS = Polycystic ovarian syndrome

Introduction

Polycystic ovary syndrome (PCOS) is one of the most widespread endocrine condition in women' reproductive age, the diagnosis of PCOS primarily relies on evaluating clinical features as the key method of identification. Additionally, the prevalence of PCOS varies across different regions, which according to recent study affects 5-20% of women throughout the reproductive age [1]. This condition is commonly associated with chronic anovulation, but some women with PCOS still ovulate, either regularly or

intermittently, insulin resistance, and elevated androgen levels. Individuals affected often seek medical care due to concerns about irregular menstrual cycles, difficulty conceiving, or excessive hair growth [2].

Apelin is a cell signaling protein released by adipose tissue that is a recently identified as adipo-cytokine. The APLN gene (endogenic ligand for the G-protein-linked receptor) codes for the peptide apelin (APLN). Researches had indicated that patients with PCOS have elevated apelin level in their serum, which is strongly correlated with both insulin resistance and body mass index (BMI) [3]. It has been established that the human ovary contains the Apelin system. In granulosa cells and oocytes, Apelin expression rises in direct proportion to the size of ovarian follicles, falls in the late luteal phase, and drastically decreases during corpus luteum (CL) regression. This biomarker may have a role in the development, maintenance, and regression of CL during the estrous cycle. Concurrently, progesterone has been shown to increase APLNR expression in granulosa cells [4]. Regarding PCOS pathophysiology, Apelin might play a role, where it takes part in the luteal phase's angiogenesis, which is connected to the growth of follicles. Luteal phase insufficiency is related to diminished progesterone production by CL. PCOS related infertility is brought on by a malfunction of CL. In women with PCOS, hyperlipidemia and insulin resistance (IR) lead to CL dysfunction and a reduction in the CL's capacity to generate and secrete progesterone [5]. Insulin like growth factor-1 (IGF-1) has been shown in recent research to be an important factor controlling ovarian follicular development and steroidogenesis in PCOS patients [6].

The main objective of the current study was to evaluate the role of Apelin serum level in women with PCOS and its correlation with obesity measured by BMI.

Methods

Study design and setting

Ninety-six adult women were involved in the study, sixty of them had been diagnosed with PCOS compared to thirty-six 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 January 2024 to June 2024.

Sample selection

A convenient sample of women in their reproductive age (20-40 years old) were enrolled in the study, who were diagnosed with PCOS, furthermore they were willing to participate, however women had a history of chronic diseases, autoimmune illness, smoking, or malignancies were excluded.

Ethical consideration

The current study was subjected to the requirements of the Helsinki Declaration. In addition, it was approved by the Ethical Committee of the College of Pharmacy, Uruk University (Official letter No. 64A dated 23/12/2023). All participants were informed about the purpose and the agreed to be enrolled.

Data collection and outcome measurements

Direct data collection from patients was done through one-on-one interviews or patient case files. Each participant signed a consent form before registration, giving access to their case file and the essential recorded data, including name, age, diseases, and medication history. Each volunteer was requested to supply 5 ml of venous blood and then placed in a tube, and centrifuged for 10-15 minutes. Apelin serum level were measured by enzyme-Linked immunosorbent assay (ELISA) analysis utilizing participant serum and specialized kit from Elabscience company with catalog number E-EL-H0456..

Statistical Analysis

The statistical analysis was performed using the statistical package for the social sciences (SPSS) version 27. Mean±standard deviation (SD) is how descriptive statistics are displayed. The patient and control outcomes of normally distributed variables were compared using the unpaired T-test. For categorical variables, Pearson's chi-squared test was used, for examining the link between parameters and outcome. The ideal cut-off value specificity, sensitivity, and area under the curve (AUC) were all measured using the receiver operating characteristic (ROC) curve.

Results

A case-control study with 96 women involved, 60 women who had been diagnosed previously with PCOS, and 36 healthy participants as a control group. There were no markable differences in weight, height, age, and BMI between the two groups (Table 1).

Table 1. Biodemographic results for the both groups

Parameter	Group	N	Mean ±SD	P value
Age (year)	Patients	60	29.9±5.05	0.751
	Control	36	30.84±5.25	
BMI (kg/m^2)	Patients	60	27.51±5.095	0.551
	Control	36	26.73±2.543	

The study showed a significant elevate in Aplin serum levels in women with PCOS when compared with controls with a P value of 0.001, as mean±SD was 486.5±51.98 pg/ml for PCOS while for control was 240.89±168.78 pg/ml (Table 2).

Table 2. Association of Apelin serum level between the two groups

Parameter	Group	N	Mean±SD	P value
Apelin (pg/ml)	Patient	60	486.5±251.98	0.001
	Control	36	240.89±168.78	

Apelin had an AUC of 0.819 which suggested it as a good diagnostic marker for PCOS patients, with a cut-off value of 206.32 pg/ml and sensitivity and specificity of 87% and 61% respectively (Table 3 and Figure 1).

The current study did not found significant correlation between Apelin serum level and BMI among PCOS patients as shown in table (4).

Table 3. Association between AUC and ROC analysis of Apelin serum level between the two groups

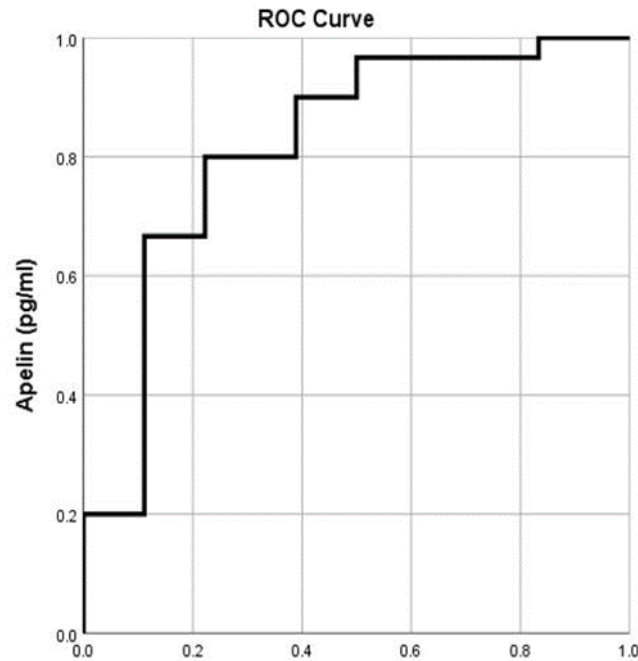| Parameter	AUC	P value	Cut-off point	Sensitivity	Specificity
Apelin(pg/ml)	0.819	<0.001	206.32	87%	61%

Figure 1. ROC analysis for Apelin in PCOS

Table 4. Pearson correlation between Apelin and body mass index in PCOS group

Parameter	Body Mass index (kg/m^2)	
	r	P value
Apelin (pg/ml)	0.101	0.495

Discussion

In the current study there is a markable positive association between Apelin serum level and PCOS with a P value of 0.001 and this was consistent with previous works, which concluded that PCOS patients had greater plasma Apelin concentrations than healthy control [8-10].

Dravecká et al. (2021) observed a positive correlation between Apelin expression in granulosa cells and follicle count, as well as in follicular fluid. The researchers found similar remarkable findings with APJ, indicating that women with PCOS and the obese group had an elevated level of this receptor's expression [11].

The current study disagreed with Gören et al. (2012), who failed to find any relevant association between PCOS women's plasma Apelin level and biochemical or clinical data, nor did they identify any in the control group [8].

The current study disagreed with Hasan Abd El Hameed (2018) and Ibrahim et al. (2018) who found that Apelin serum levels decreased in

women with PCOS compared to healthy women with a positive relationship with BMI. [10,12] Choi (2012) found that women with PCOS who had or hadn't hyperandrogenism both showed Significantly decrease in serum Apelin level when compared to controls [13].

This study found no correlation between Apelin serum level and BMI. Apelin is a ligand of the APJ receptor that comes in three distinct forms, Apelin-36, Apelin-17, and Apelin-13, depending on the cleavage location. In addition to being expressed by adipocytes, additional tissues that also express it include skeletal muscle, the stomach, the lung, the brain, and the heart. In this case, Apelin concentrations and BMI did not significantly correlate. This result probably indicates the range of physiological functions that Apelin is involved in, rather than that Apelin is secreted as an Adipokine that uniquely identifies unhealthy adipose tissue [14]. The finding of this study agreed with Castan-Laurell I et al. (2012) who suggested that there is no correlation between Apelin level and BMI [15].

A meta-analysis encompassing eighty-one trials revealed no discernible variations in Apelin level in women with PCOS and normal BMI relatives to healthy controls with comparable BMI [16]. Varying outcomes throughout the published research could be related to variations in age, ethnicity, study design, genetic traits, and evaluation techniques [9]

The limitation of this study is that modest sample sizes for both groups may have led to conflicting results; as a result, larger cohorts with distinct genetic origins are needed for future research.

In conclusions, Apelin may represent a BMI-independent marker of PCOS, underscoring its potential relevance in disease pathophysiology. The observed elevation highlights the need for further studies to clarify its mechanistic role and evaluate its utility in diagnosis or management..

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Conflict of interest

The author declare there is no conflict of interest.

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