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Assessment of Atrial natriuretic peptide serum level in patients with polycystic ovary syndrome in Iraqi population

Maryam Ahmed Abdulrahman [1], Sami. A. Zbaar [2]

[1] Ministry of Health.
[2] Department of Biochemistry, Faculty of Medicine, Tikrit University

Corresponding Author Email: Dr.samizbar@tu.edu.iq

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Abstract

Background: Polycystic ovarian syndrome is a prevalent metabolic condition in women of reproductive age. The prevalence rate is approximately 9% among women of reproductive age. This study sought to assess the levels of atrial natriuretic peptide in patients with PCOS and its correlation with insulin resistance and hyperandrogenism.

Methods: 60 patients with PCOS were screened to be suitable for participation in this study, aged from 19 to 45. They were attended to at the outpatient clinic, as well as 30 healthy women as a control group. Serum levels of insulin, testosterone, and corin were estimated using an ELISA kit, as well as glucose, FSH, LH, and HbA1c.

Results: The present study revealed that there are no significant differences in ANP serum level between PCOS patients and the healthy control group. As well as it showed an increase in the corin levels, although corin is part of its function, which is to activate the ANP. In addition, the study demonstrated that the plasma ANP was directly correlated with insulin resistance and the LH/FSH ratio.

Conclusions: The results of this study emphasize the importance of NP and Corin serum levels in women with PCOS. Our data suggest that circulating corin reflects the metabolic abnormalities of PCOS patients. We also discovered a robust positive association between the ANP level and insulin resistance.

Introduction

Polycystic ovarian syndrome (PCOS) is a multifaceted metabolic endocrine condition that has recently become a predominant cause of infertility in women worldwide. The prevalence rate among women of reproductive age ranges from 8% to 13%. [(1).] The diagnosis and management of PCOS is a complex task due to its enigmatic nature and significant symptoms that fluctuate with age. [(2).] The diagnosis and management of PCOS is a complex undertaking due to its enigmatic nature and significant symptoms that fluctuate with age. [(3)]. Numerous scientific studies have demonstrated that various conditions, including obesity, atherosclerotic dyslipidemia, systemic inflammation, oxidative stress, insulin resistance, abnormal glucose homeostasis, and hormonal alterations, significantly influence the pathophysiology of polycystic ovary syndrome. [(4)] Ascertaining the precise cause and effect of PCOS is exceedingly challenging due to its numerous intricacies. It is defined by a condition in which multiple elements, including hereditary and environmental influences, interact.

ANP was initially identified by de Blod in 1981. It is predominantly synthesized in the heart's atrial and constitutes 98% of the circulating natriuretic peptides. Secreted ANP is swiftly eliminated from circulation via binding to particular clearance receptors and

breakdown by neutral endopeptidases. ANP serves as an autonomous metabolic route that contributes to the regulation of exercise-induced lipolysis. ANP has been identified as playing a role in the control of various ovarian physiological processes in animal models, including ovarian steroidogenesis and oocyte maturation. while a low amount of ANP was reported The mechanism underlying this drop in PCOS patients remains unestablished. It may pertain to factors within adipose tissue or the ovary.

Material and methods

This cross-sectional study was conducted in the Department of Obstetrics and Gynecology at al-yarmouk general hospital in Baghdad City from the 1st of September 2024 to the 30th of January 2025. 60 patients with PCOS were screened to be suitable for participation in this study, aged from 19 to 45. Women were included in this study. The patients were diagnosed with polycystic ovary syndrome. They have been attended to at outpatient clinics and were included in this study, as well as 30 healthy subjects as a control group. Their ages ranged between 20 and 45, matching with the patients group. All PCOS patients were diagnosed based on the presence of two of the Rotterdam criteria. Patients with endocrine and metabolic disorders like diabetes and thyroid disease were excluded from this study. After midnight, a fast 5 ml blood sample has been taken from all participants. To perform the serum levels of the following (ANP, corin, FSH, LH, insulin, glucose, and testosterone). The study will be conducted on both patients and healthy control groups.

Ethical approval was obtained from the Ethical Committee of the College of Medicine at Tikrit University. A written, dated, and signed informed consent was obtained from all subjects after explaining the nature and purpose of this study.

Results

In polycystic ovarian patients as showed in table (4-1), 45 patients (75%) were married and 15 patients (25%) were unmarried 8 patients (14%) from rural areas and 52 patients (86%) from as; 38 patients (63 %) es and 22 and 22 patients (37%) ents 24 patients (40%) were hirsutism and 36 patient (60%) shown in as shown in table 1.

Table 1 showed the characteristics of PCOS patients and control groups

characteristics		Patients		control	
		No.	%	No.	%
Marital status	Married	45	75%	23	76%
	Single	15	25%	7	24%
Residence	Rural	8	14%	5	17%
	Urban	52	86%	25	83%
Previous birth	yes	38	63%	24	80%
	No	22	37%	6	20%
Hirsutism	absent	24	40%	25	83%
	present	36	60%	5	17%
Period pattern	Normal	20	33%	27	90%
	poly	6	10%	0	0%
	oligo	22	37%	3	10%
	Amenorrhea	12	20%	0	0%

The current study established that menstrual cycle irregularity is prevalent among women with PCOS. The fraction of women with PCOS who can conceive is diminished. Acne and hirsutism were the predominant findings in this study, corroborating prior research indicating that around 80% of women with PCOS exhibit hirsutism.

The current study indicated that women with PCOS exhibited a higher prevalence of overweight and obesity compared to those without the condition, highlighting the major impact of BMI on the pathophysiology of PCOS development.

Table 2: demonstrates the Corin serum level regarding BMI.

BMI		Corin level pg/ml	
		Patients	control
Underweight	18<	2406 ± 917	1900 ± 854
Normal	18.5-24.9	2867 ± 1153	2346 ± 653
Overweight	25- 29.9	2685 ± 987	2545 ± 916
Obese	30>	4380 ± 1232	2687 ± 785
P value		Sig	Non sig

This study showed that serum level of FSH in PCOS patients was decreased than that of normal healthy women). the main metabolic feature of PCOS is hormonal changes so the decreased serum level of FSH laying with this manner and mainly depend on characteristics of patients itself

Table 3: show the differences in mean and SD. Of some biochemical parameters between PCOS patients and healthy control subjects.

Parameters	GROUPS	No.	Mean	Std. D	P Value
TESTOSTERONE	PATIENTS	60	57.69	11.98	Sig
	CONTROL	30	42.56	13.14	
IR	PATIENTS	60	4.15	1.57	Sig
	CONTROL	30	2.46	.5478	
Corin	PATIENTS	60	3095.7	1072.90	Sig
	CONTROL	30	2332.8	1031.6	
ANP	PATIENTS	60	445.8	217.6	non-Sig
	CONTROL	30	534.3	278.4	
INSULIN	PATIENTS	60	13.97	3.20	Sig
	CONTROL	30	11.14	2.31	

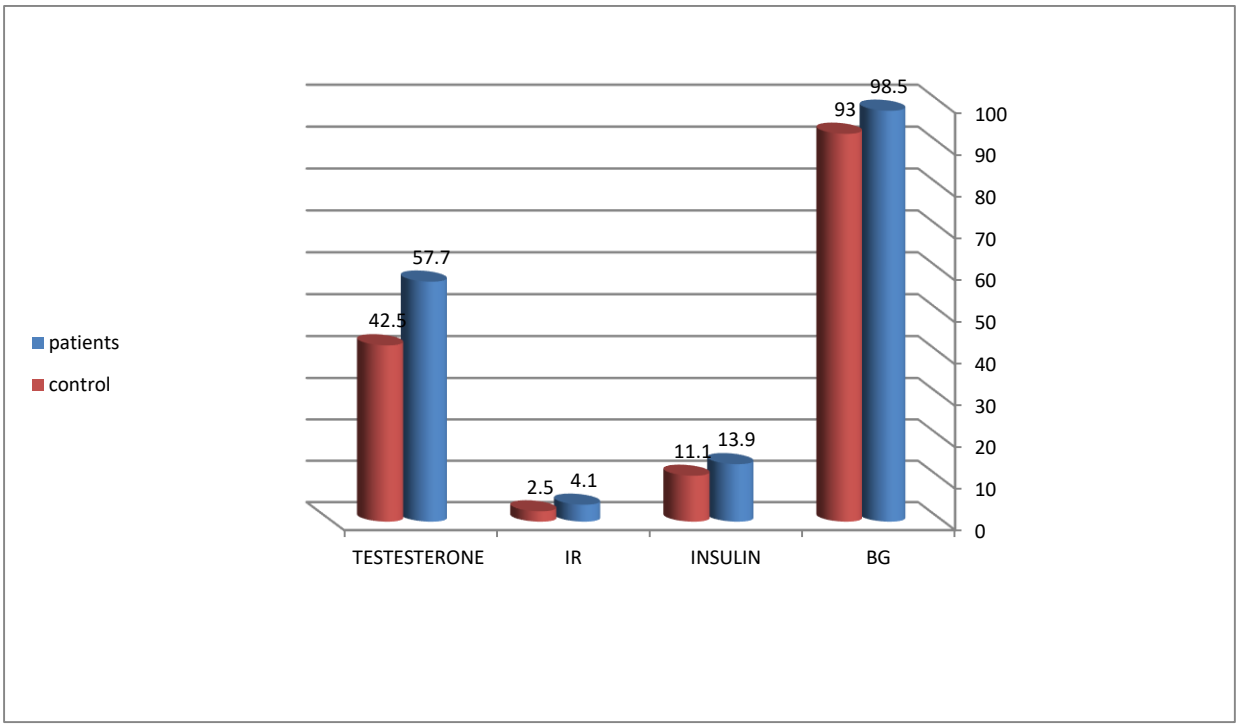

Figure 1: demonstrate the differences of (Testosterone, IR, INSULIN, BG) in PCOS patients and control group

Regarding the serum levels of Corin the present study revealed that the is a significant differences in corin level between the PCOS patients and healthy control group.

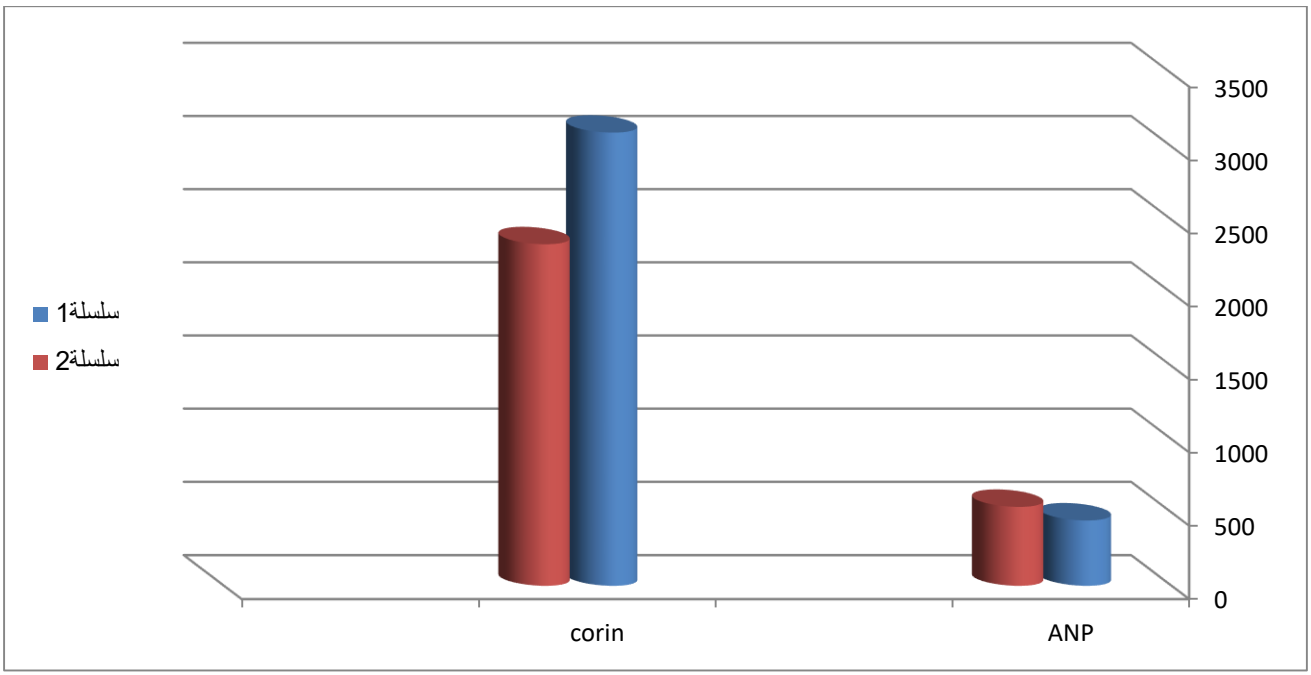

Figure 2: show the differences in Corin and ANP serum levels in PCOS patients and control group.

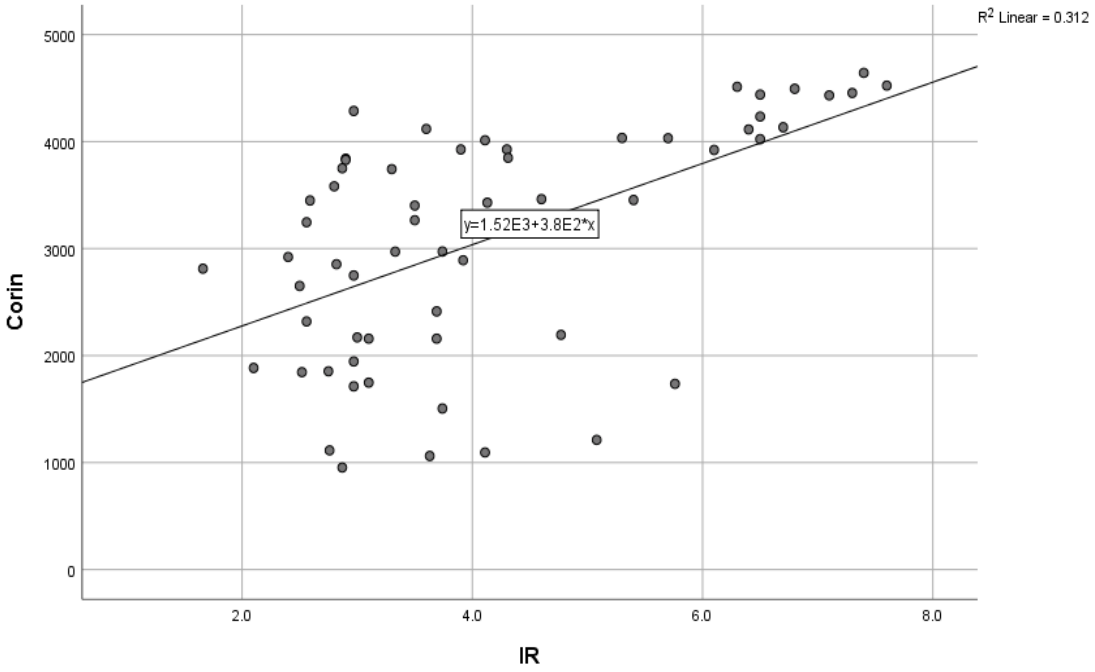

Figure 3: show the correlation between IR and Corin serum levels in PCOS patients' group.

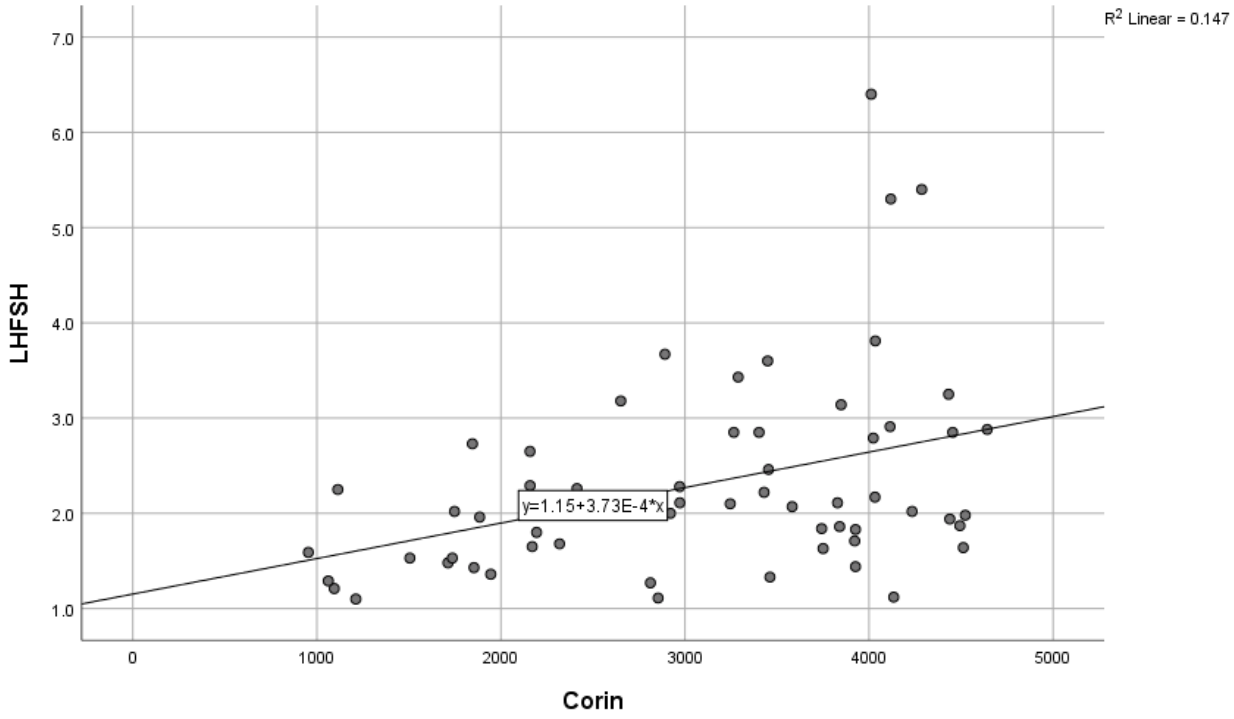

Figure 4: show the correlation between LH/FSH ratio and Corin serum levels in PCOS patients' group

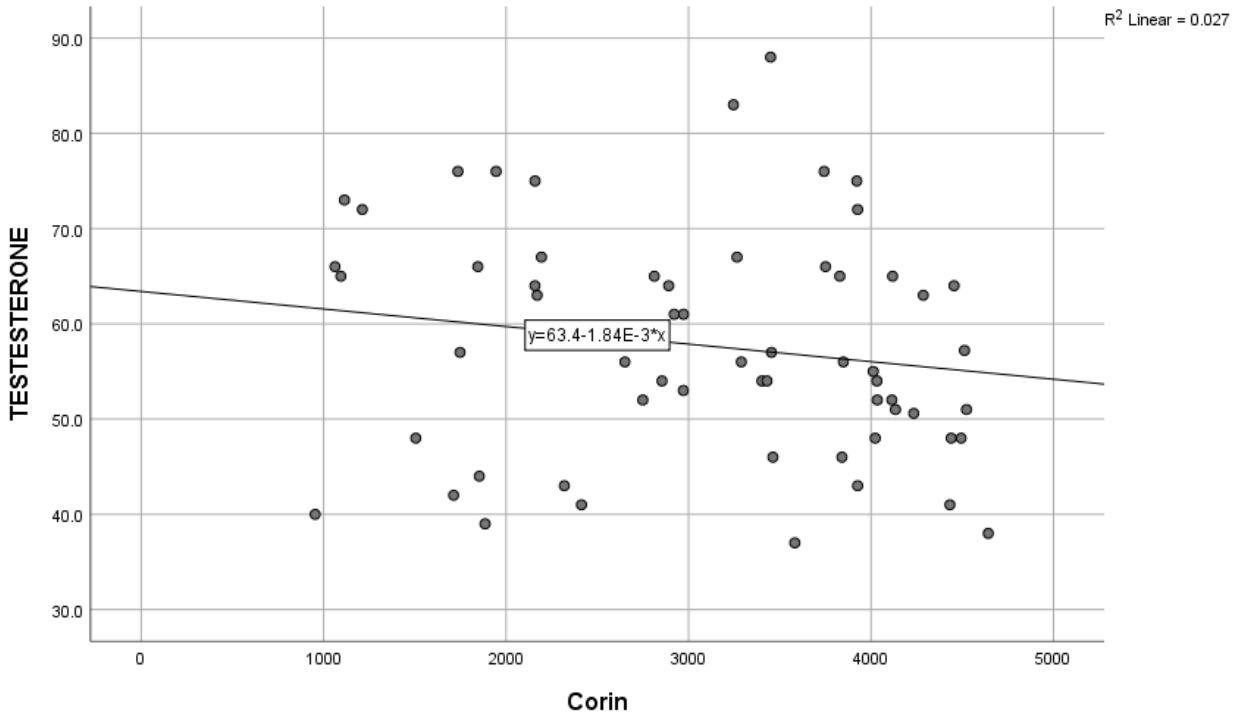

Figure 5: show the correlation between testosterone and Corin serum levels in PCOS patients' group

Discussion

The current study established that menstrual cycle irregularity is prevalent among women with PCOS. The fraction of women with PCOS who can conceive is diminished. Acne and hirsutism were the predominant findings in this study, corroborating prior research indicating that around 80% of women with PCOS exhibit hirsutism. The prevalent symptoms linked to PCOS mostly arise from increased serum concentrations of androgens, particularly testosterone and SHBG. These heightened levels result in hirsutism of facial

hair, acne, alopecia, seborrhea, and obesity. .[8] Elevated testosterone levels contribute to the manifestation of PCOS symptoms, including infertility, polycystic ovaries, hirsutism, and acne. The findings of this study concur with those of Trummer et al. (2015). [9] and (Omer ZS .et al ,2018). [10].

The current investigation indicated that there are no significant differences in ANP serum levels between PCOS patients and healthy control women, with ANP levels being non-significantly lower in patients compared to controls. These findings are consistent with prior studies. [11,12]. Introduced by Moro et al. in 2009 and Lauria et al. in 2013, it was confirmed that the reduction in ANA levels in women with PCOS was not correlated with age or obesity, suggesting that ANP plays a role in the pathology of PCOS itself. The mechanism by which ANP is involved in PCOS remains unclear, potentially relating to factors in adipose tissue or the ovary. Some have proposed an increase in its receptor gene expression in adipose tissue. [13]. It is presumed that the ovulatory dysfunction associated with PCOS leads to a reduction in ovarian ANP, as demonstrated in mouse models of polycystic ovary syndrome. The involvement of ANP in the regulation of oocyte meiosis, maturation, and ovarian steroidogenesis is demonstrated by animal studies and the association between its levels in follicular fluid and the quantity of follicles aspirated for in vitro fertilization. [14]. Atrial natriuretic peptide (ANP) is predominantly synthesized by atrial myocytes, which play crucial roles in controlling acid-base equilibrium, blood pressure, and body fluid homeostasis due to its pharmacological effects on natriuresis and diuresis. Furthermore, it was also identified in ovarian oocytes and granulosa cells. [15]. ANP produced from the ovary can modulate ovarian activities, including follicular development and hormone synthesis, via autocrine or paracrine mechanisms. [16].

ANP binds to natriuretic peptide receptor A, a subtype of guanylyl cyclase receptor, converting GTP into cyclic GMP. cGMP elicits actions, including vasodilation and enhanced natriuresis, to lower systemic blood pressure. [17]. cGMP may also modify the effects of the RAAS and the sympathetic nervous system. ANP augments the p38 MAPK-PGC1α-UCP1 signaling pathway in human and murine adipocytes. Consistently, lower phosphorylation of p38 MAPK and diminished amounts of PGC1α and UCP1 proteins were seen in the iBAT of corin knockout mice. [18].

Besides the p38 MAPK-PGC1α-UCP1 pathway, several molecular pathways contributed to natriuretic peptide-induced activation of brown adipose tissue. The activation of the mammalian target of rapamycin complex 1 is an additional signaling pathway in BNP-mediated adipose browning in human adipocytes. [19]. Furthermore, given the hormone's association with obesity, it may influence the progression of the disease in other manners. Natriuretic peptide clearance receptors (NPR-C) are prevalent in adipose tissue, indicating that adipocytes are involved in the elimination of natriuretic peptides from the bloodstream. [20].

This study demonstrated elevated levels of Corin in women with PCOS relative to healthy women, concurrently revealing a reduction in ANP levels, despite Corin's role in activating ANP. Consequently, we infer that additional mechanisms may implicate Corin in the pathophysiology of PCOS beyond the established mechanism of ANP activation. Multiple hypotheses have been posited regarding Corin's involvement in the pathogenesis of PCOS, encompassing its association with insulin resistance, obesity, and hyperglycemia. All of these factors are involved in the etiology of the disease in one way or another. Moreover, corin resistance refers to the diminished response to the available corin, prompting the body to enhance its secretion in reaction to stimuli.

To activate the heart and show when the corin is working, the body produces natriuretic peptides. People who are overweight tend to have lower levels of natriuretic peptides. People who are overweight may experience corin resistance. [19] HK-2 cells lacking corin showed decreased eNOS activity, increased MAPK activity, and poor motility. Results were similar when ANP-siRNA transfection was used, indicating that Corin influences ANP. In metabolic disorders, endothelial dysfunction occurs as a result of MAPK and eNOS activation, and in Reno, Corin plays a protective role by digesting pro-ANP. [20].

The activity of corin may not rise correspondingly in obese persons, despite elevated levels of corin in this population. Measuring corin activity is essential to investigate the correlation between corin and obesity.

In line with earlier research by Peng et al. [21] this examination confirmed a direct relationship between Plasma Corin and BMI. Studies conducted by Peng et al. found a strong association between Corin and body mass index (BMI), total cholesterol (TC), and low-density lipoprotein (LDL-C). The LH/FSH ratio was significantly related to DHEA-S. An indicator of polycystic ovary syndrome (PCOS) is the LH-FSH ratio. The correlation between Corin and the LH/FSH ratio was positive, showing that it was a very sensitive and specific indicator of polycystic ovary syndrome (PCOS). [22]

Anovulation is the main cause of infertility in PCOS, however the exact process is still unclear. It revealed that Corin was a significant independent predictor of PCOS infertility. Rather of being linked to fat, high Corin levels are linked to infertility in polycystic ovary syndrome (PCOS). [23]. High Corin levels were associated with a 5.9-fold increased risk of infertility in PCOS patients compared to low Corin levels. The complex relationship between insulin sensitivity and gonadal activity is just one of many well-documented relationships between PCOS, obesity, and metabolic syndrome. Obstructive obesity and altered adipokine production are common symptoms of metabolic syndrome and may shed light on the underlying pathophysiology of infertility. [24].

Conclusion

The study indicated that the majority of women with PCOS were aged between 20 and 45. The findings of our study underscore the significant importance of Corin serum levels in women with PCOS. Our observations indicate that circulating Corin reflects the metabolic anomalies in people with PCOS. It was also disclosed that a robust positive association exists between corin levels and insulin resistance. The study indicates a considerable increase in insulin resistance in PCOS patients compared to the healthy control group.

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Conflicts of Interest

All authors declare no conflicts of interest, financial or otherwise, related to this work.

Ethical approval: obtained from the Ethical Committee of College of medicine -Tikrit University. A written dated and sign informed consent was obtained from all subject after explanation the nature, purpose of this study.

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