

Assessment Of Corin Serum Level In Patients With Polycystic Ovary Syndrome A Cross-Sectional Study

Maryam Ahmed Abdulrahman¹, Sami A Zbaar²

¹ Ministry of health.

² Department of Biochemistry, Faculty of Medicine, Tikrit University

Abstract

Background: Polycystic ovary syndrome is one of the most common metabolic disorder in women with reproductive age group. With a prevalence rate of nearly 9% among women with reproductive age. This study aimed to evaluate the Corin serum level in patients with PCOS and its relation 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 women they have been attended to outpatients clinic as well as 30 healthy women as a control group Serum level of insulin, testosterone and Corin were estimated, using an ELISA kit, as well as glucose, FSH, LH and HbA1c have been calculated.

Results: the present study revealed that there is a significant differences in Corin serum level between PCOS patients and healthy control group. As well as it showed a decrease in the ANP levels, although Corin is part of its function, which is to activate the ANP. In addition the study demonstrated that the Plasma Corin was directly correlated with BMI and LH/FSH ratio.

Conclusions: The results of this study emphasize the important role of Corin serum level in women with PCOS. Our data suggest that circulating Corin reflect the metabolic abnormalities PCOS patients. Also revealed that there was a strong positive correlation between corin level and insulin resistance.

Key words. PCOS, Corin, Insulin resistance, hyperandrogenism and ANP.

INTRODUCTION

Polycystic ovary syndrome (PCOS), It is a complex metabolic endocrine disorder that has recently emerged as one of the leading causes of infertility in women globally. its prevalence rate is from 8–13% of reproductive age women⁽¹⁾. The diagnosis and management of PCOS is a challenging endeavor because it is a mysterious condition with major symptoms that vary with age⁽²⁾. The early diagnosis of the disease has profound effect on the treatment and management of the disease so many researchs focusing on biochemical parameters that may have a role in early diagnosis of PCOS⁽³⁾. Many scientific evidences revealed that there are many disease include Obesity, atherosclerotic dyslipidemia, systemic inflammation, oxidative stress, insulin resistance, abnormal glucose homeostasis as well as hormonal changes have a profound effect in pathophysiology of polycystic ovary syndrome,⁽⁴⁾ Determining the exact cause and effect of PCOS is very difficult due to its many complexities. It is characterized by a disease in which several factors interact, including genetic and environmental factors.

Corin is a type II transmembrane serine protease, which is mainly expressed in atrial and ventricular cardiomyocytes. Corin is a key enzyme in the natriuretic peptide (NP) system. There are two types of pro-atrial natriuretic peptide (pro-ANP). Serum corin is a well-known biomarker of cardiovascular disease and chorin activity in the heart^(5,6), but its role in patients with other common diseases has not yet been elucidated and there are no studies in this area. In recent years, some studies have found that low levels of atrial natriuretic peptides are associated with an increased risk of diabetes.⁽⁷⁾ This finding suggests a potential effect of atrial natriuretic peptides on diabetes. As a physiological activator of atrial natriuretic peptides, corin may be associated with diabetes.

MATERIAL AND METHODS

This cross sectional study was conducted in the Department of Obstetrics and Gynecology al-yarmouk general hospital in Baghdad city from the 1 September 2024 to the 30th 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 poly cystic ovary syndrome, they have been attended to outpatients clinic were included in this study as well as 30 healthy subjects as a control

group their age were ranged between (20-45) 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 fast 5 ml of blood sample has been taken from all participants. To perform the serum levels of the following (FSH , LH, Insulin , glucose, testosterone and Corin). In patients and healthy control groups. Ethical approval was 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.

Results

In polycystic ovarian patients as showed in table (4-1) , 45 pateints (75%) were married and 15 patients (25%) were un married , 8 pateints (14%) from Rural and 52 patients (86%) from Urban ,38 patients (63 %) having baby and 22 patients (37%) non , 24 patients (40%) were hirsutism and 36 patient (60%) were non hirsutism as shown in table (4.1)

Table (4-1) 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 present study confirmed that that menstrual cycle irregularity was common in women suffering from PCOS. As well as the percentage of PCOS women who have the ability to have children is reduced . Acne and hirsutism was also the most common finding in this study, which agrees with other studies of hirsutism among women with PCOS, which is around 80%.The current study showed that women with PCOS were an overweight and obese more than normal which demonstrate the significant effect of BMI in pathophysiology of PCOS development

.Table (4-4) demonstrate the Corin serum level regarding to BMI

	BMI	Corin level pg/ml	
		Patients	control
Under weight	<18	2406 ± 917	1900± 854
Normal	18.5 -24.9	2867 ± 1153	2346 ± 653
Over weight	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 mianly depend on characteristics of patients itself

Table (4-6) 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
TESTESTERONE	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	
LH/FSH ratio	PATIENTS	60	2.30	1.04	Sig
	CONTROL	30	1.42	0.33	
INSULIN	PATIENTS	60	13.97	3.20	Sig
	CONTROL	30	11.14	2.31	

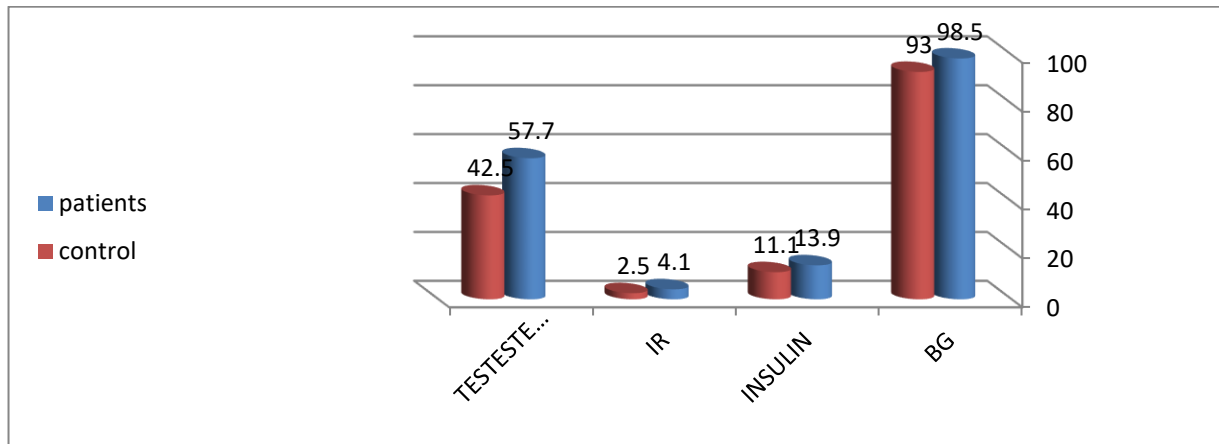


Figure (4-2) demonstrate the differences of (Testosterone , IR , INSULIN , BG) in PCOS patients and control group

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

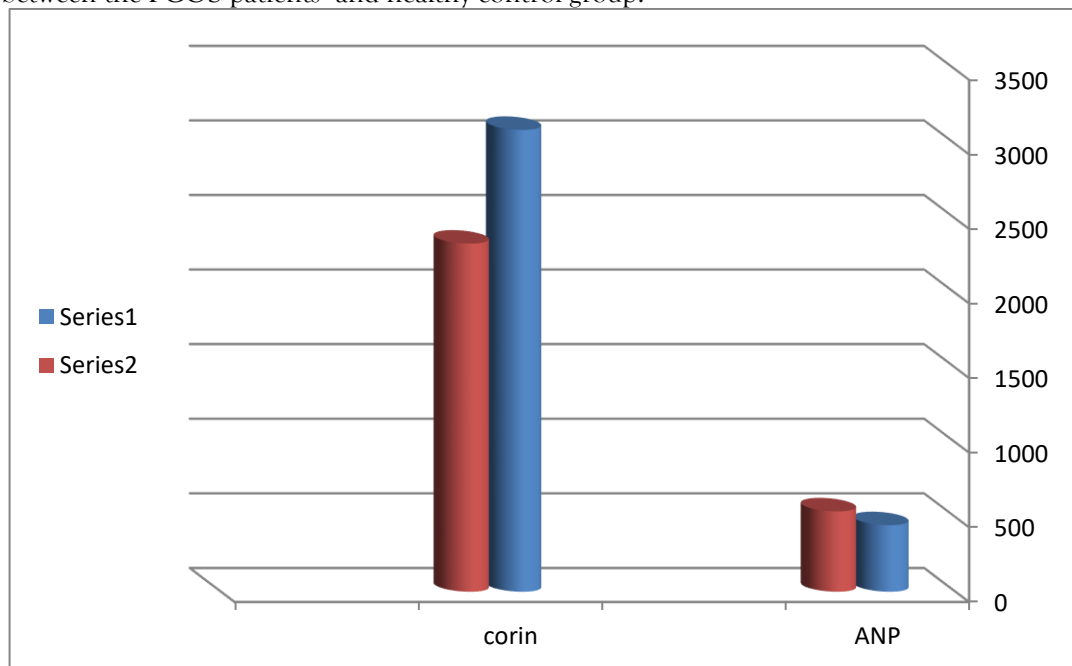


Figure (4-3) show the differences in Corin and ANP serum levels in PCOS patients and control group

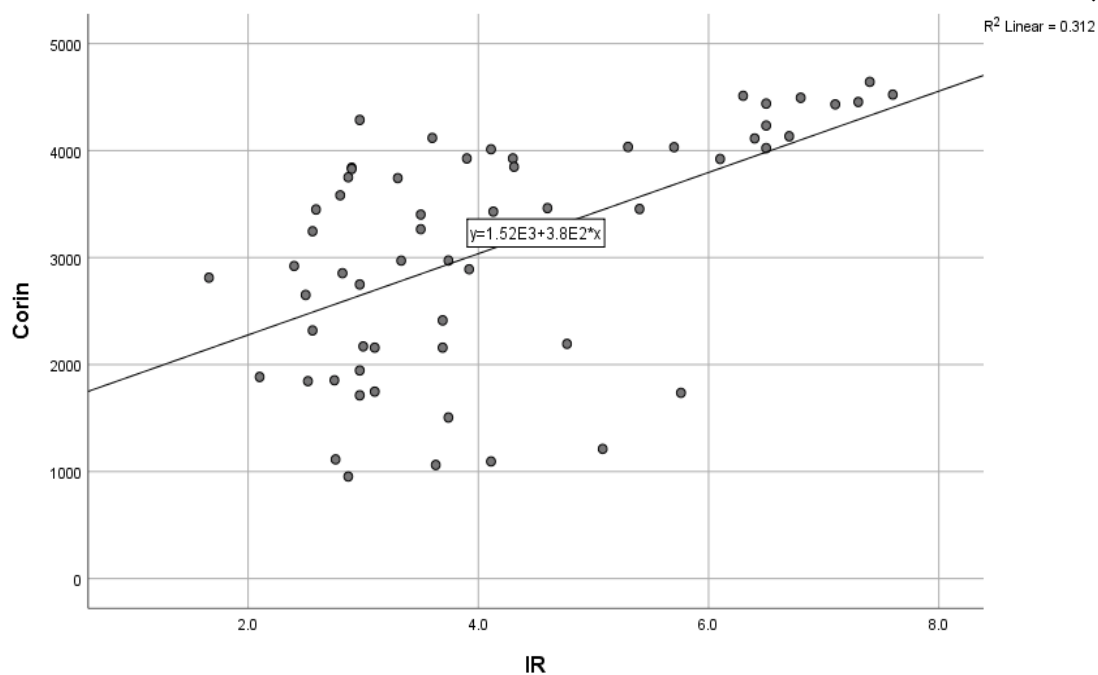


Figure (4-4) show the correlation between IR and Corin serum levels in PCOS patients group.

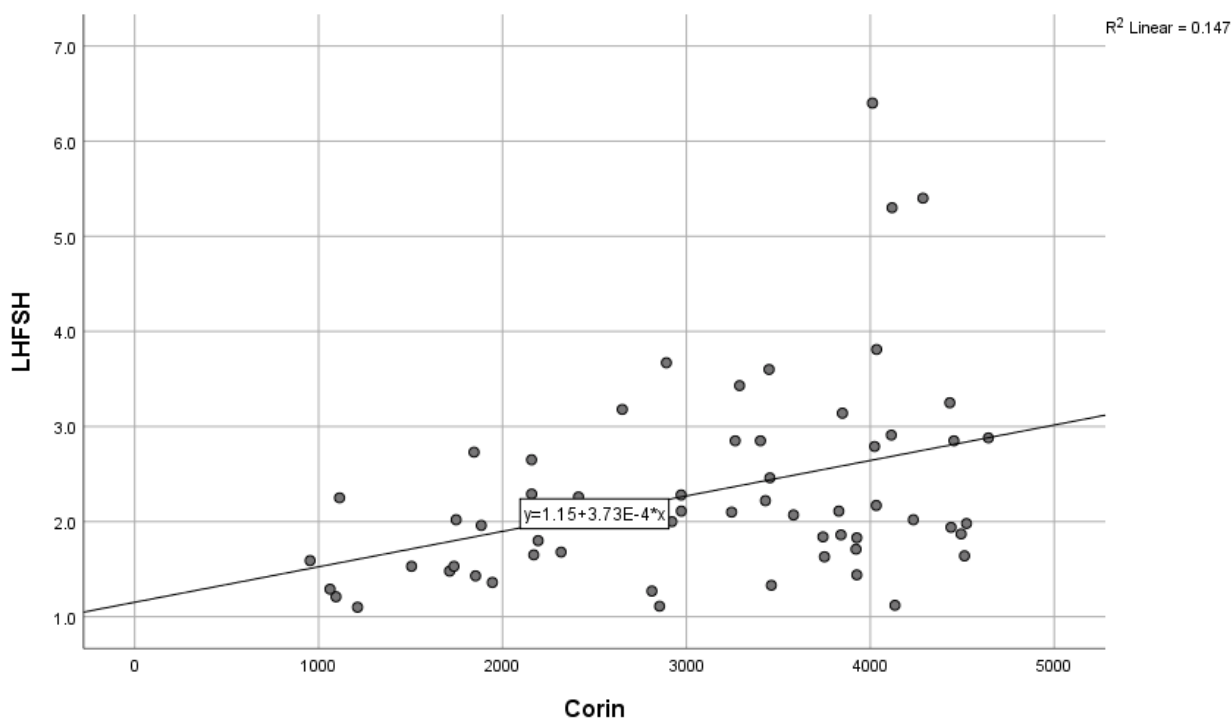


Figure (4-6) show the correlation between LH/FSH ratio and Corin serum levels in PCOS patients group

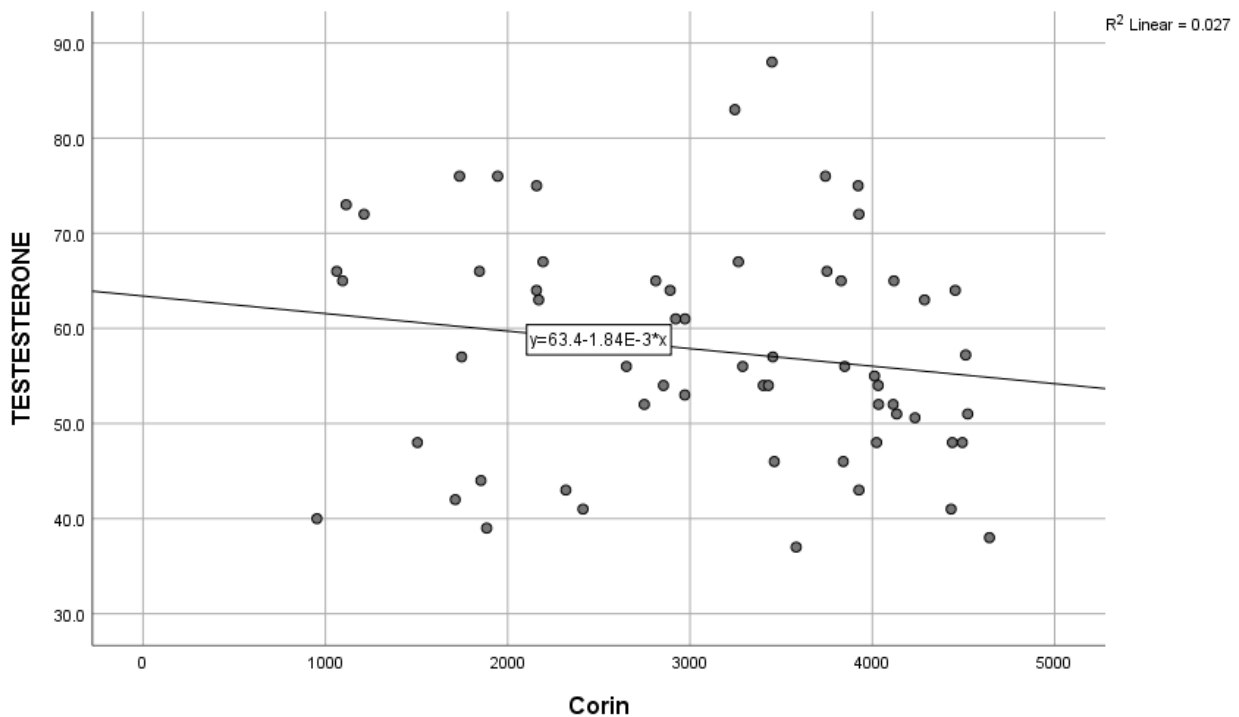


Figure (4-7) show the correlation between testosterone and Corin serum levels in PCOS patients group

DISCUSSION

The present study confirmed that that menstrual cycle irregularity was common in women suffering from PCOS. As well as the percentage of PCOS women who have the ability to have children is reduced . Acne and hirsutism was also the most common finding in this study, which agrees with other studies of hirsutism among women with PCOS, which is around 80% . The common symptoms associated with PCOS which most commonly occur due to elevated serum levels of androgens, specifically testosterone and SHBG. These elevated levels lead to hirsutism of facial hair, acne , alopecia, oily skin and obesity .⁽⁸⁾ High testosterone levels are one of the causes that lead to the development of PCOS symptoms including infertility, polycystic ovaries, hirsutism, and acne. This study's findings were in agreement with (Trummer C. et al, 2015).⁽⁹⁾ and(Omer ZS .et al ,2018).⁽¹⁰⁾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 in agreement with Mohamed Abdel et al.⁽¹¹⁾ who stated that Corin level was significantly higher in PCOS patients than that of control group . the role of Corin in various physiological and pathological processes including PCOS remains unclear and still not been evaluated yet there are many research suggesting its role in development in diabetes and other metabolic disorders . Although the role of Corin in polycystic ovary syndrome has only been evaluated by just one study⁽⁷⁵⁾ , the role of corin and its relationship with insulin resistance has been confirmed by many studies. Given the important relationship between insulin resistance and the development of polycystic ovary syndrome, so the assumption of a relationship between corin and PCOS has become justified⁽¹²⁾ . There are many evidences support our hypothesis , Corin may participate in the regulation of adipose tissue morphology and function as well as endothelial dysfunction , Corin mediated-ANP activation is an important hormonal mechanism in regulating adipose tissue function and body temperature upon cold exposure in mice⁽¹³⁾ . Corin and ANP can regulate adipose metabolism and function via a local autocrine mechanism⁽¹⁴⁾). Corin mRNA does not expression in mouse WAT, BAT, and SVF-derived adipocyte , these results suggest that the Corin and ANP-mediated regulation of adipose tissue function may be via an endocrine but not autocrine mechanism in mice⁽¹⁵⁾ . Recently, corin mRNAs were found to be expressed in human mesenchymal stem cells from adipose tissue ⁽¹⁶⁾ which would differentiate into adipocytes, suggesting a potential role of Corin in production of adipose as well as corin may promote the differentiation of mesenchymal stem cells into adipocytes. The previous study revealed that Corin serum levels were increased in PCOS and were directly related with the Rotterdam criteria. Therefore, Corin could have

a important role in PCOS pathophysiology⁽¹⁷⁾. also they found that levels of corin mRNA and protein in uterus were significantly lower in preeclamptic women than in normal pregnancies, whereas plasma soluble corin levels were higher in preeclamptic patients than in non-pregnant or normal pregnant women. In addition to the inconsistent corin levels between circulation and tissues, corin activity might be a contribution to the conflicting findings⁽¹⁸⁾. This study showed an increase in the levels of Corin in women with PCOS compared to healthy women, at the same time, it showed a decrease in the ANP levels, although Corin is part of its function, which is to activate the ANP. Therefore, we conclude from the above that there may be another mechanisms by which Corin involve in the pathophysiology of the PCOS other than the known mechanism, which is ANP activation. There are several hypotheses proposed through which Corin can participate in the development of the PCOS, which include the relationship of chorine to insulin resistance, obesity and hyperglycemia. As it was known, all of these factors involve by way or another in the pathogenesis of the disease. In addition, there is what is called corin resistance, which means there is a lack of response to the existing corin, and thus the body increases As a physiological activator of natriuretic peptides, natriuretic .its secretion in response to stimuli. peptides can be used as an indicator of corin activity. Natriuretic peptides levels were found to be decreased in obese individuals. So there may be a phenomenon of corin resistance among obese individuals⁽¹⁹⁾. Corin-deficient HK-2 cells had inhibited migration, increased MAPK activity, and decreased eNOS activity. Similar effects were observed with ANP-siRNA transfection indicating that Corin mediates its effects through ANP. From all mention previously Corin plays a Reno protective role through pro-ANP processing, and defects in Corin cause endothelial dysfunction through MAPK and eNOS signaling in metabolic disorders⁽²⁰⁾. Activity of corin may be not increased proportionally in obese individuals although the level of corin is increased in obese individuals. It is more important that activity of corin should be measured to study the relationship between corin and obesity. This study confirmed that the Plasma Corin was directly correlated with BMI which come in consisted with another study introduce by Peng et al.⁽²¹⁾. stated that Corin was significantly correlated with BMI, total cholesterol, and LDL-C. The correlation between the LH/FSH ratio and DHEA-S was significant. LH-FSH ratio contributed as a diagnostic tool for PCOS. Corin showed a positive correlation with the LH/FSH ratio, but it had higher specificity and sensitivity for PCOS prediction⁽²²⁾. PCOS infertility is mainly attributed to anovulation, but its underlying mechanism is still uncertain. Corin appeared to be a significant independent predictor of infertility in PCOS patients. High Corin contributed to PCOS infertility, not to obesity correlation⁽²³⁾. The probability of infertility was greater (5.9-fold) in PCOS patients with high Corin levels compared to those who had low Corin levels. Beyond the well-known links between PCOS, obesity, and metabolic syndrome, gonadal functions, and insulin sensitivity exhibit complex relationships. Important pathophysiological connections between metabolic syndrome and infertility may be explained by standard types of dysfunctional adiposity and altered adipokine production⁽²⁴⁾.

CONCLUSION

The study showed that the majority of PCOS women were in age between 20 -45. The results of our study emphasize the important role of Corin serum level in women with PCOS. Our data suggest that crculating Corin reflect the metabolic abnormalities PCOS patients. also revealed that there was a strong positive correlation between corin level and insulin resistance. Als the study demonstrate that there was significant increase in insulin resistance in PCOS patients than that of healthy control group

REFERENCES

- 1.Bednarska S, Siejka A. The pathogenesis and treatment of polycystic ovary syndrome: What's new? *Adv Clin Exp Med.* 2017;26(2):359-67.
- 2.Salim J, Khalaf, Moayad M. Al Anzy. Impact of Metformin On Osteoprotegerin levels In Polycystic Ovarian Women. *GMN;*2024; 1 (346) 2024:144-146
- 3.ihad AT Levels of AMH and Hecpidin as Potential Biomarkers for Polycystic Ovary Syndrome. *Georgian medical news.*2023; 6 (339):47-51.Tawfeq MT. Metformin effects on neuregulin-1 in polycystic ovarian women. *Georgian medical news.* 2023;4:56-6.
- 4.Semenov AG, Tamm NN, Seferian NN, Postnikov KR, Karpova AB, Serebryanaya NS, Koshkina DV, Krasnoselsky EV, Katrukha MI. Processing of pro-B-type natriuretic peptide: furin and Corin as candidate convertases. *Clin Chem.* 2010;56(7):1166-76.

- 5.Zhang X, Gu X, Zhang Y, Dong N, Wu Q. Corin: a key mediator in sodium homeostasis, vascular remodeling, and heart failure. *Biology*. 2022;11(5):717.
- 6.Yu R, Han X, Zhang X, Wang Y, Wang T. Circulating soluble corin as a potential biomarker for cardiovascular diseases: a translational review. *Clin Chim Acta*. 2018;485:106-12.
- 7.Sami A. Zbaar, Sawsan S. Hosi, Doaa Sabeeh Al-Nuaimi. Association of Nestatin-1 resistance in obese adolescents of Iraq population. *Gorgian medical news*. 2023;No10 (343) 107-110
- 8.Trummer C, Schwetz V, Giuliani A, Obermayer-Pietsch B, Lerchbaum E. Impact of elevated thyroid-stimulating hormone levels in polycystic ovary syndrome. *Gynecol Endocrinol*. 2015;31(10):819-23.
- 9.Omer ZS, Ahmied MS, Yaqoub NK. Relation of visfatin and polycystic ovarian syndrome in women. *Med J Babylon*. 2018;15(4):316.
- 10.Mohamed Abdel-moniem Ibrahim , Amira Saber Al-Karamany , Marwa M. Esawy3 , Amina Nagy Elasy. Plasma Corin: A New Biochemical Marker for Polycystic Ovary Syndrome. *Reproductive Sciences (2024)* 31:2219-2227
- 11.Sarhat ER, Abid IM, Kamel NA, Sarhat TR, Abass KS. Changes of serum Interleukin and Chemerin levels in patients with Polycystic Ovary syndrome. *J Adv Pharm Educ Res*. 2021;11(4):11- 4. <https://doi.org>
12. Xianrui Zhang , Wenguo Li , Tiantian Zhou , Meng Liu , Qingyu Wu , Ningzheng Dong. Corin Deficiency Alters Adipose Tissue Phenotype and Impairs Thermogenesis in Mice. *Biology (Basel)*. 2022 Jul 23;11(8):1101
- 13.Meiting Xue , Yue Shi , Aiming Pang , Li Men , Yahui Hu , Pengfei Zhou . et al. Corin plays a protective role via upregulating MAPK and downregulating eNOS in diabetic nephropathy endothelial dysfunction. *FASEB J*. 2020 Jan;34(1):95-106.
- 14.Dong, L.; Wang, H.; Dong, N.; Zhang, C.; Xue, B.; Wu, Q. Localization of corin and atrial natriuretic peptide expression in human renal segments. *Clin. Sci*. 2016, 130, 1655-1664.
- 15.Zhou H, Liu W, Zhu J, Liu M, Fang C, Wu Q, et al. Reduced serum corin levels ipatients with osteoporosis. *Clin Chim Acta* 2013;426:152-156.
- 16.Zaki MA, El-Banawy SE-DS, El-Gammal HH. Plasma soluble corin and N-terminal pro-atrial natriuretic peptide levels in pregnancy induced hypertension. *Pregnancy Hypertension: Int J Women's Cardiovascular Health* 2012;2:48-52.
- 17.Sami A. Zbaar, Islam K. Kamal, Atyaf Alchalabi. Association between serum level of adipokines in patients with prostate cancer. *Gorgian medical news*. 2024;No12(357)173-177.
- 18.Chen S, Sen S, Young D, Wang W, Moravec CS, Wu Q. Protease corin expression and activity in failing hearts. *Am J Physiol Heart Circ Physiol* 2010;299:H1687-H1692.
- 19.Meiting Xue, Yue Shi, Aiming Pang, Li Men, Yahui Hu, Pengfei Zhou, Guangfeng Long. Corin plays a protective role via upregulating MAPK and downregulating eNOS in diabetic nephropathy endothelial dysfunction. *FASEP j*.2020. VOL.24.1: 95-106