

Article

# The Relationship Between Fetuin-A and Glycemic Control in Women with Polycystic Ovary Syndrome in Babylon Province

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**Abstract:** Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age and is strongly associated with insulin resistance and infertility. This study aimed to evaluate serum Fetuin-A levels and their relationship with glycemic control and reproductive hormones in women with PCOS. A case-control study was conducted on 90 women aged 18–44 years in Babylon Province, Iraq. Participants were divided into two groups: 45 obese infertile women diagnosed with PCOS and 45 healthy controls. Serum levels of Fetuin-A, kisspeptin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), fasting insulin, and fasting blood glucose were measured using ELISA techniques. Insulin resistance was assessed using the homeostatic model assessment (HOMA-IR). The results revealed a significant increase in serum Fetuin-A, fasting insulin, LH, HOMA-IR, and LH/FSH ratio in PCOS patients compared with controls ( $P < 0.05$ ). In contrast, kisspeptin and FSH levels were significantly decreased. Fetuin-A showed a strong positive correlation with fasting insulin and HOMA-IR and a significant negative correlation with kisspeptin. In conclusion, elevated Fetuin-A levels are closely associated with insulin resistance and hormonal imbalance in PCOS, suggesting its potential role as a biomarker in the pathogenesis of the syndrome.

**Keywords:** PCOS, Fetuin-A, Insulin Resistance, HOMA-IR, Kisspeptin.

## Introduction

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology [1], [2]. It represents one of the leading causes of infertility among women of reproductive age. In addition to reproductive abnormalities, PCOS is frequently associated with metabolic disturbances, particularly insulin resistance, which increases the risk of developing type 2 diabetes mellitus [3].

Fetuin-A is a glycoprotein synthesized primarily in the liver and is known to inhibit insulin receptor tyrosine kinase activity, thereby contributing to insulin resistance [3], [8]. Elevated circulating levels of Fetuin-A have been linked to metabolic disorders, including obesity and type 2 diabetes. Therefore, it may play a significant role in the pathophysiology of PCOS.

Kisspeptin is a neuropeptide encoded by the KISS1 gene and plays a crucial role in regulating the hypothalamic–pituitary–gonadal axis [4], [11]. It influences gonadotropin-releasing hormone (GnRH) secretion and consequently affects LH and FSH levels. Alterations in kisspeptin signaling may contribute to hormonal imbalance in PCOS.

The aim of this study was to evaluate serum Fetuin-A levels and investigate their relationship with glycemic control and reproductive hormones in women with PCOS.

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## Materials and Methods

**Study Design and Participants** This case-control study included 90 women aged 18–44 years recruited from Babylon Teaching Hospital for Maternity and Children and private clinics in Al-Hillah city between September 2023 and February 2024. Participants were divided into two groups: 45 women diagnosed with PCOS and 45 healthy controls.

### Inclusion Criteria

- Women diagnosed with PCOS
- Age between 18–44 years

### Exclusion Criteria

- Hypertension
- Thyroid disorders
- Use of hormonal medications

**Biochemical Analysis** Blood samples were collected after overnight fasting. Serum levels of Fetuin-A, kisspeptin, LH, FSH, and insulin were measured using enzyme-linked immunosorbent assay (ELISA) kits. Fasting blood glucose was also determined.

**Assessment of Insulin Resistance** Insulin resistance was evaluated using the homeostatic model assessment index (HOMA-IR).

**Statistical Analysis** Data were expressed as mean  $\pm$  standard deviation (SD). Statistical analysis was performed using SPSS version 20. Student's t-test and Pearson correlation analysis were used to assess differences and relationships between variables. A P-value  $< 0.05$  was considered statistically significant.

**Ethical Approval** The study protocol was approved by the Scientific Committee of the Department of Biochemistry, College of Medicine, University of Babylon. Verbal informed consent was obtained from all participants.

### Results

Significant differences were observed between PCOS patients and the control group. Serum levels of Fetuin-A, fasting insulin, LH, HOMA-IR, and LH/FSH ratio were significantly higher in patients compared to controls ( $P < 0.05$ ). In contrast, serum kisspeptin and FSH levels were significantly lower in the PCOS group.

Correlation analysis demonstrated a strong positive association between Fetuin-A and fasting insulin, as well as HOMA-IR. Additionally, Fetuin-A showed a moderate positive correlation with fasting blood glucose. A significant negative correlation was observed between Fetuin-A and kisspeptin levels. Furthermore, kisspeptin was negatively correlated with LH and the LH/FSH ratio, while showing a positive correlation with FSH.

**Discussion** The findings of the present study demonstrate that women with PCOS exhibit significant metabolic and hormonal alterations, including elevated Fetuin-A levels and increased insulin resistance. These results support the hypothesis that Fetuin-A plays a critical role in the development of insulin resistance by inhibiting insulin receptor signaling pathways [3], [8].

The observed increase in fasting insulin and HOMA-IR further confirms the presence of insulin resistance in PCOS patients. This is consistent with previous studies indicating that insulin resistance is a central feature in the pathogenesis of PCOS [14].

The decrease in kisspeptin levels observed in this study may reflect dysregulation of the hypothalamic–pituitary–gonadal axis. Kisspeptin is known to regulate GnRH secretion, and its reduction may contribute to altered gonadotropin release, particularly the imbalance between LH and FSH [4], [10].

**Table 1.** Biochemical characteristics of control and PCOS groups.

Parameter	Group	Mean $\pm$ SD	P-value
Fetuin-A (ng/L)	Patients	423.05 $\pm$ 30.2	<0.05
	Control	230.4 $\pm$ 12.3	
Kisspeptin (ng/L)	Patients	270.2 $\pm$ 16.7	<0.05
	Control	295.9 $\pm$ 13.2	
FSH (mIU/ml)	Patients	3.7 $\pm$ 0.3	<0.05
	Control	6.8 $\pm$ 0.9	
LH (mIU/ml)	Patients	8.5 $\pm$ 1.1	<0.05
	Control	4.9 $\pm$ 0.81	
LH/FSH Ratio	Patients	2.1 $\pm$ 0.7	<0.05
	Control	0.69 $\pm$ 1.3	
HOMA-IR	Patients	6.09 $\pm$ 1.08	<0.05
	Control	2.35 $\pm$ 1.05	
Fasting Insulin (IU/ml)	Patients	20.5 $\pm$ 2.2	<0.05
	Control	10.3 $\pm$ 1.7	
FBG (mg/dl)	Patients	80.5 $\pm$ 1.4	<0.05
	Control	73.2 $\pm$ 2.3	

The elevated LH/FSH ratio observed in PCOS patients is a well-established hormonal characteristic of the syndrome [7]. This imbalance may result from increased GnRH pulse frequency, which preferentially stimulates LH secretion over FSH.

**Table 2.** Correlation between studied parameters.

Correlation	r	P-value
Fetuin-A vs Kisspeptin	-0.7	<0.05
Fetuin-A vs FBG	0.5	<0.05
Fetuin-A vs Fasting Insulin	0.81	<0.05
Fetuin-A vs HOMA-IR	0.45	<0.05
Kisspeptin vs LH	-0.78	<0.05
Kisspeptin vs FSH	0.59	<0.05
Kisspeptin vs LH/FSH	-0.82	<0.05

Overall, the correlations identified in this study highlight the interconnected relationship between metabolic and reproductive dysfunction in PCOS, with Fetuin-A acting as a potential link between insulin resistance and hormonal imbalance.

The findings of the present study demonstrate that women with PCOS exhibit significant metabolic and hormonal alterations, including elevated Fetuin-A levels and increased insulin resistance. These results support the hypothesis that Fetuin-A plays a critical role in the development of insulin resistance by inhibiting insulin receptor signaling pathways.

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### Conclusion

Elevated serum Fetuin-A levels are strongly associated with insulin resistance and hormonal disturbances in women with PCOS. These findings suggest that Fetuin-A may serve as a useful biomarker in understanding the pathogenesis and potential diagnosis of PCOS.

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