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Hormonal and metabolic factors accompanied polycystic ovary syndrome among Iraqi women and its association with zinc deficiency

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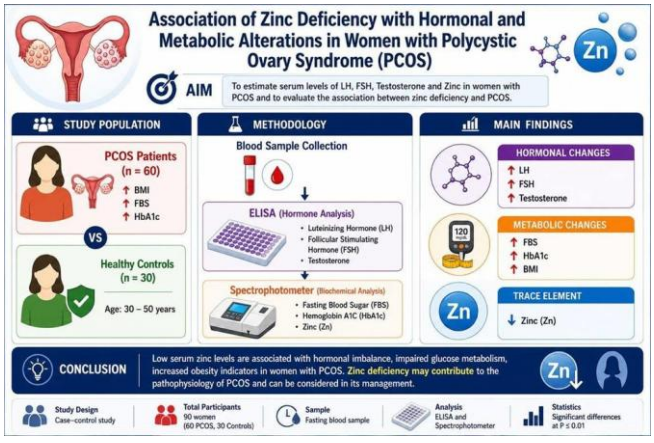
Abstract

Polycystic ovary syndrome (PCOS) is a common hormonal disorder characterized by irregular menstrual periods, elevated androgen (male hormone) levels, and small, fluid-filled sacs on the ovaries. While there is no cure, symptoms can be effectively managed with diet, exercise, and medications. This study aimed to estimate serum luteinizing hormone, testosterone and follicular stimulating hormone levels for patients suffering from polycystic ovary syndrome. Also, shed light on the association of polycystic ovary syndrome with zinc levels by measuring serum levels of zinc. A total of 60 women patients with ages ranging between 30 and 50 years from an outpatient clinic specializing in gynecological surgery in Baghdad suffering from polycystic ovary syndrome, also were taken thirty healthy for comparison in this study. For biochemical parameters fasting blood sugar test, hemoglobin A1C, were determined by spectrophotometer. Hormone levels were determined by the ELISA technique. The results indicated a substantial increase ($p \leq 0.01$) in blood levels of FBS, HbA1c, and body mass index in PCOS patients compared to healthy women. Results of hormone parameters also showed that significant increase in hormone levels and a decline ($p<0.01$) in serum levels of zinc (Zn) for PCOS patients in comparison with controls.

Keywords: Polycystic ovary syndrome (PCOS). Testosterone (Testo). Luteinizing hormone (LH), Follicular stimulating hormone (FSH).

Graphical Abstract



Source: Own authorship.

Introduction

Anovulation, infertility, obesity, polycystic ovaries, and insulin resistance are prevalent hallmarks of polycystic ovarian syndrome (PCOS). Overweight, gut dysbiosis, neuroendocrine disorders, genetics, lifestyle, environmental pollutants, and lifestyle or nutrition are among the risk factors for PCOS in women **[1]**. The previously mentioned conditions may lead to the

deteriorating of metabolic syndrome by causing oxidative stress, hyperinsulinemia, hyperandrogenism, and diminished folliculogenesis, ultimately leading to irregular menstrual periods **[2]**. According to a systematic screening of women utilizing the National institute of Health (NIH) diagnostic guidelines, 5-10% of women who are in reproductive-age.

Although PCOS can occur at any age, starting with menarche, the majority of cases occur between the ages of 20 and 30 **[3]**. Hyperandrogenism, ovarian morphology, and anovulation are the three main criteria used to diagnose PCOS, according to international recommendations **[4]**.

The development, appearance, and management of PCOS may be influenced by a variety of environmental factors, such as geography, nutrition and diet, socioeconomic status, and pollutants in the environment **[5]**. Insulin is a peptide hormone created by beta cells that are linked to pancreatic islets. It governs the metabolism of carbohydrates, lipids, and proteins by facilitating the uptake of glucose from the bloodstream into adipose, hepatic, and skeletal muscle cells **[6]**.

The role of pancreatic beta cells was release insulin into the bloodstream. When blood glucose absorption is elevated, a reduction in blood glucose levels suppresses insulin secretion. Testosterone is considered as the principal male sex hormone and is associated with anabolic steroids.

Hyperandrogenemia refers to elevated androgen levels associated with menstrual cycle irregularities and various adverse metabolic characteristics, including central obesity, insulin resistance, dyslipidaemia, and chronic inflammation in premenopausal women, all of which contribute to an increased cardiovascular risk. Furthermore, researchers discovered that approximately 80% of women with hyperandrogenism also polycystic ovary. Zinc is a vital trace element necessary as a catalytic, functional, and regulatory ion for the function of over 300 enzymes, proteins, and transcription factors **[7]**. Consequently, zinc is regarded as a crucial element that contributes to numerous homeostatic interactions in the body, encompassing various biological processes. Zinc maintains constant levels of hormones such as oestrogen, testosterone, and progesterone during the menstrual cycle.

This study aimed to estimate serum luteinizing hormone, testosterone and follicular stimulating hormone levels for patients suffering from polycystic ovary syndrome. Also, shed light on the association of polycystic ovary syndrome with zinc levels by measuring serum levels of zinc.

Pathogenesis

Globally, PCOS impacts 8% to 20% of women of reproductive age each year, based on the analytic standards **[8]**. The pathophysiology of this disorder is affected by changes in steroidogenesis, ovarian follicle development, neuroendocrine function, metabolism, secretion of insulin, insulin sensitivity, adipocyte activity, mediators of inflammation, and sympathetically nerve function **[9]**. In PCOS, ovarian follicles fail to mature properly, leading to anovulation (absence of ovulation) **[10]**. Lifestyle alteration and weight loss have established efficacy in reducing androgen effects, enhancing ovulation, and boosting the sensitivity to insulin **[11]**.

Methods

In this study, a total of 90 women subjects were included, 60 of them were symptomatic newly diagnosed patients with polycystic ovary syndrome of ages ranging from 30 to 50 years who attended the outpatient clinic specializing in gynecological surgery of Yarmouk teaching hospital in Baghdad from the period from March to June 2024. The rest 30 were considered as apparently healthy women. All of them was diagnosed by ultrasonography. The sample size was selected based on the availability of suitable participants and with reference to previously published studies with similar objectives and designs.

Blood samples were taken from individuals who had recently been diagnosed with polycystic ovary syndrome (PCOS) (60) and from women who appeared to be in good health (30). The control group consisted of women between the ages of 30 and 50 who did not have polycystic ovary syndrome (PCOS) but were visiting the case department for other minor diseases. A number of women were excluded from the study, including those who were already taking supplements prior to the evaluation, as well as those who had type 2 diabetes, thyroid illness, imbalanced prolactin, or other metabolic conditions, pelvic inflammatory disorders, or any other metabolic condition. During the second to fifth day of the menstrual cycle. Blood samples were obtained via venipuncture by using a 5 mL plastic disposable. anticoagulant-free vacutainer, blood samples were leave to clot at room temperature. After 2 hours at 24 °C. Afterwards, the serum was rotated for 5 minutes at about 5000 rpm to separate it. It was subsequently moved to a sterile vial and labeled with the patient's name and the date of collection so it could be used in biochemical testing. First, we used HbA1C to measure fasting blood sugar. The levels of luteinizing hormone (LH), follicle- stimulating hormone (FSH), and testosterone were measured using the i-

CHROMATM HbA1c, which is based on fluorescent immunoassay technology and chemiluminescence assay. A computerized clinical chemistry autoanalyzer AU 680 (Beckman Coulter Inc., USA) based on the concept of colorimetry/photometry was used to measure the serum zinc levels.

The datasets generated during the current study are not publicly available due to confidentiality and privacy restrictions but are available from the corresponding author upon sensible request and with permission from the related institution.

Ethical Approval

This study was approved in March 2025 by the Ethics Committee of the Commission Industrial Applications & Materials Technology Research Center under approval number 156/0008, in accordance with the Declaration of Helsinki and its 2024 updates. Informed consent was applicable.

Statistical Analysis

Statistical analysis was performed using the Statistical Analysis System (SAS) software package, version 2012. Data were obtainable as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was used to evaluate the significance of differences among the study groups. When a significant effect was observed, the Least Significant Difference (LSD) test was employed as a post hoc analysis to compare group means. A probability value of $p \leq 0.01$ was considered statistically significant.

Results and Discussion

According to the findings of the study, there are differences in the values of the fasting blood level, the HbA1c level, and some hormones such as testosterone, LH, and FSH. As well as when comparing this result between women with PCOS and normal women.

The study demonstrated a statistically significant rise ($p \leq 0.01$) in the weight of patients (89.3 ± 8.6) compared to the control group (58.80 ± 7.6). A highly substantial increase ($p \leq 0.01$) in fasting blood levels (32.33) was seen simultaneously in fasting blood level (157.3 ± 15.8) while in healthy women (91.7 ± 7.6), also increase in HbA1C levels in PCOS in comparing with control. The glucose concentration in PCOS patients exhibited an elevated level at $p < 0.01$ compared to control women (Table 1).

Table 1. Levels of weight, Body mass index (BMI), Fast blood sugar (FBS), and Hemoglobin A1c (HbA1C) between PCOS and normal women.

parameters	Mean ± SE		p-value
	PCOS n=60	Control n=30	
weight	89 ± 8.6	58.6 ± 4.7	0.01
BMI	28.5 ± 2.1	23.4 ± 1.9	0.01
FBS mg/dL	157 ± 15.8	91.7 ± 7.9	0.01
HbA1C	8.1 ± 1.5	5.4 ± 1.1	0.01

Source: Own authorship.

Additionally, the findings of this study indicated a notable increase in the weight of women with PCOS relative to normal women. Our results align with those of **[12]**, who reported that almost all of women with PCOS are obese, in contrast to normal women. They are closely correlated with both PCOS and obesity, since analogous genes may contribute to adiposity in people afflicted with PCOS **[13,14]**. Our results showed an increase significantly in the level of blood glucose and insulin resistance (Figure 1).

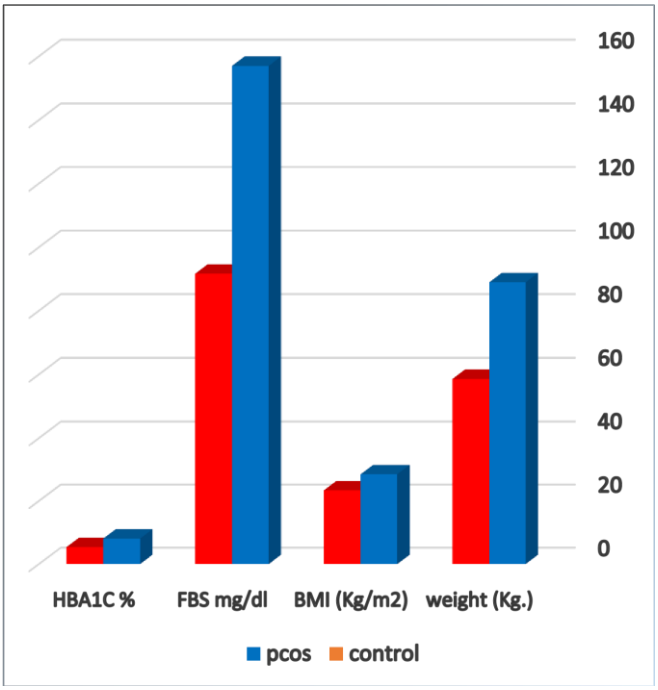


Figure 1. Levels of weight, Body mass index (BMI), Fast blood sugar (FBS), and Hemoglobin A1c (HbA1C) between PCOS and normal women. Source: Own authorship.

When compared to the control group, the zinc level in the PCOS group was substantially lower (65.68±31.28) compared to the control group (82.56±9.84), with a p-value of 0.01 (Table 2).

Table 2. Serum zinc level for PCOS and control group.

Parameters	Mean ± SE		p-value
	(PCOS) 60	control 30	
Zinc level mg/dL	67.82	83.9	0.01

Source: Own authorship.

There was a contrast between this study and another one that was conducted by **[15]**, which found that there was no significant difference among the patient's group and the control group in terms of zinc levels in the blood ($p>0.05$). In contrast to the results of zinc level between healthy and PCOS women as in Figure 2. Zinc is a powerful antioxidant, and an absence of it causes enhanced oxidative damage in various organs, particularly the heart **[16]**. This is one of the possible reasons that zinc's association to polycystic ovary syndrome (PCOS) may be about. Other than triggering insulin system problems, zinc may also have an effect on oxidative stress.

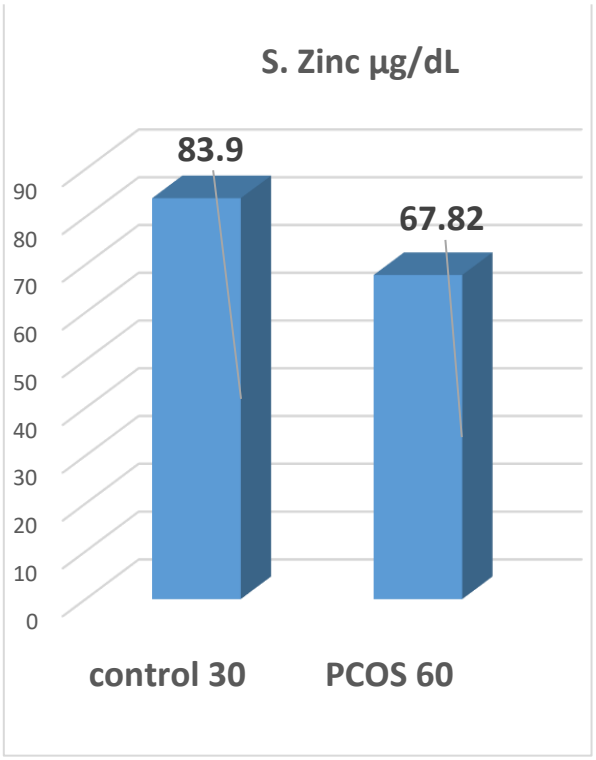


Figure 2. Serum zinc levels in PCOS and normal women. Source: Own authorship.

In addition, the testosterone hormone concentration was significantly higher in women with polycystic ovary syndrome (224.8 ± 71.2) compared with healthy women (46.7 ± 9.4), with a p-value of less than 0.01 (Table 3).

Table 3. Levels of Testosterone, luteinizing hormone (LH), follicular stimulating hormone (FSH) between PCOS and normal women.

parameters	Mean ± SE (PCOS) 60	Control 30	p-value
Testo. mg/mL	224±71.2	46.7 ± 9.4	0.01
LH MIU/L	9.79±1.72	5.91 ± 1.67	0.01
FSH MIU/L	3.9±0.62	6.83 ± 0.87	0.01

Source: Own authorship.

Insulin may not be sensitive enough to the estimated risk of polycystic ovary syndrome (PCOS) in women, according to the study, which raises testosterone levels in combination with high glucose levels. In this study, like in the previous one, women with polycystic ovary syndrome (PCOS) and hyperinsulinemia also had elevated testosterone levels, which may be higher than the normal range or even slightly higher **[17]** found an abnormally high amount of testosterone in PCOS, which is supported by this study. Thus, testosterone is crucial for the diagnosis of polycystic ovary syndrome **[18]**. This LH imbalance leads to impaired ovarian function, contributing to anovulation, androgen excess, and the formation of cystic follicles **[19]** (Figure 3).

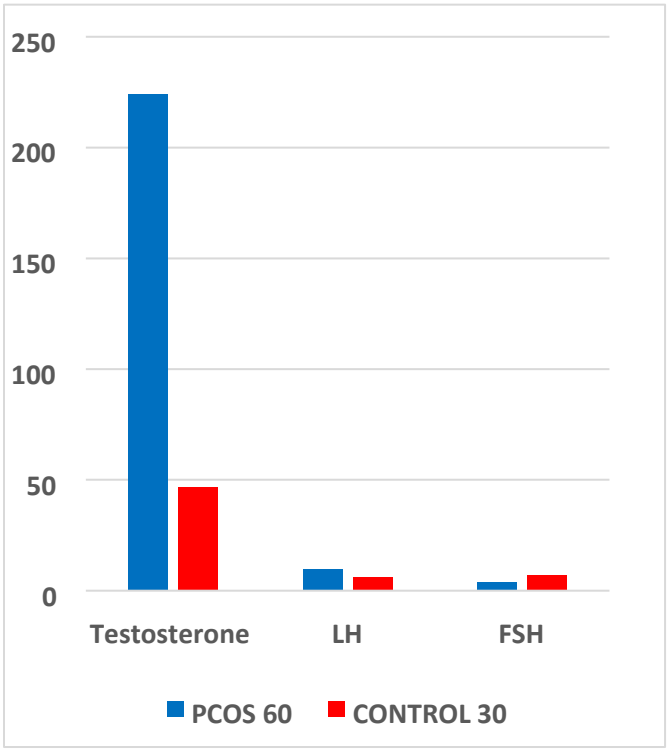


Figure 3. Testosterone, luteinizing hormone (LH), follicular stimulating hormone (FSH) levels in PCOS and normal women. Source: Own authorship.

Authors found that PCOS women had elevated insulin levels during the luteal phase, therefore our findings are in line with theirs. Increased insulin levels inhibit progesterone synthesis by granulosa cells isolated from PCOS women, according to **[20]**, but this effect is absent in normal women. The study's findings demonstrated that T, LH, and FSH were occupied in PCOS subjects.

The four main factors that cause patho-physiological changes in polycystic ovary syndrome (PCOS), as stated by **[21]**, are an excess of carbs in the diet, high insulin levels, an increase in male hormone production, and chronic low-grade

inflammation. The data show that zinc levels drop along with polycystic ovarian syndrome. These findings were derived from a different study that also found that PCOS patients' serum zinc levels were significantly lower **[22]**. At the same time, research has shown that insulin levels are positively correlated with LH concentrations during the phase of luteal development **[23,24]**.

Limitation

This study has several limitations. First, the moderately small sample size and recruitment of participants from a single hospital may limit the generalizability of the results. Second, certain potential confounding factors, including dietary habits, lifestyle characteristics were not evaluated. In addition, the cross-sectional design of the study precludes founding a causal relationship between serum zinc levels and polycystic ovary syndrome. Therefore, further large-scale, multicenter, and longitudinal studies are suggested to confirm these findings and clarify the underlying mechanisms.

Conclusion

The findings of this study show that women with polycystic ovary syndrome (PCOS) exhibited significantly lower serum zinc levels compared with healthy controls. This association suggests that zinc deficiency may play a role in the pathophysiology of PCOS through its effects on oxidative stress, and hormonal imbalance. insulin resistance. Therefore, monitoring zinc status and considering appropriate nutritional interferences may contribute to improving the management of PCOS. Further large-scale studies are recommended to explain the underlying mechanisms and evaluate the therapeutic benefits of zinc supplementation in women with PCOS.

CRediT

Author contributions: Conceptualization, methodology, investigation, data collection, laboratory work, formal analysis, data interpretation, writing—original draft: All authors; Supervision: Suhaib Raad Qasim.

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Ethical Approval

This study was approved in March 2025 by the Ethics Committee of the Commission Industrial Applications & Materials Technology Research Center under approval number 156/0008, in accordance with the Declaration of Helsinki and its 2024 updates.

Informed Consent

It was applicable.

Funding

Not applicable.

Data Sharing Statement

The datasets created and analyzed during this study are available upon reasonable request from the responsible author.

Conflict of Interest

The authors declare no competing interests.

Similarity Check

It was applied by Ithenticate[@].

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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