Assessment of Serum Zinc Level in Women with Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a prevalent endocrine-metabolic disorder affecting 6-10% of women of reproductive age. While the pathophysiology of PCOS remains complex, recent studies suggest trace elements, such as zinc, may play a significant role in its development and management.

Objectives: This study aimed to assess the relationship between serum zinc levels and the presence of PCOS among women visiting the outpatient clinics at Basrah Maternity and Children's Hospital.

Methods: A prospective case-control study was conducted from October 2023 to September 2024, involving 150 women: 50 diagnosed with PCOS and 100 healthy controls. Participants were stratified by body mass index (BMI) and serum zinc levels were measured. Statistical analyses were performed using SPSS version 26, employing Chi-square tests for categorical variables and independent t-tests for continuous variables, with a significance level set at $p \leq 0.05$.

Results: The study revealed significantly lower serum zinc levels in women with PCOS compared to controls (63.8 ± 20.6 µg/dL vs. 76.8 ± 22.7 µg/dL, $p = 0.002$). In the PCOS group, those with obesity demonstrated even lower zinc levels (60.71 ± 3.01 µg/dL vs. 71.2 ± 5.4 µg/dL in obese controls, $p = 0.024$). Furthermore, elevated luteinizing hormone (LH) levels were observed in PCOS women, correlating with lower zinc levels.

Conclusions: The findings indicate a significant association between reduced serum zinc levels and the presence of PCOS, particularly in obese women. This suggests that zinc deficiency may exacerbate the hormonal imbalances characteristic of PCOS, highlighting the importance of monitoring zinc status in managing this syndrome.

Keywords: Assessment, Serum, Zinc Level, Polycystic Ovary Syndrome.

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Introduction

Polycystic ovary syndrome (PCOS) is a prevalent endocrine-metabolic disorder in women of reproductive age. It can be characterised by various hormonal imbalances, leading to symptoms of hyperandrogenism that have a significant impact on female health in the short and long term. (1) It affects 6–10% of women who are of reproductive age. In the general population, its prevalence ranges from 5–10%, and among obese women, it is over 30%. (2)

Functional ovary hyperandrogenism (FOH) is the primary cause of nearly all polycystic ovary syndrome (PCOS) cases, present in two-thirds of them. FOH is characterized by abnormal androgen production and an exaggerated 17-hydroxyprogesterone (17-OHP) response to gonadotropin stimulation. Atypical FOH cases lack this exaggerated 17-OHP response but may show increased testosterone after adrenal androgen suppression. About 3% of PCOS cases have isolated functional adrenal hyperandrogenism. The

remaining PCOS cases are typically mild and often associated with obesity, which may explain their atypical steroid secretion profiles. (3) Polycystic ovary syndrome is diagnosed by the presence of a minimum of two of the following: (4) Signs or symptoms of elevated androgens (unwanted facial or body hair, hair loss from the head, acne, or high blood testosterone levels) after ruling out other potential causes. Irregular or absent menstrual cycles after excluding other potential causes. The presence of polycystic ovaries was detected through an ultrasound scan. PCOS is diagnosed by ruling out other illnesses that have similar symptoms. These conditions include thyroid illness, hyperprolactinemia, and non-classical congenital adrenal hyperplasia. If some individuals have clinical symptoms indicating other potential causes, they may need a more thorough investigation. (5) Zinc is a crucial micronutrient that is necessary for a variety of important biological processes. It is an essential constituent of several enzymes and proteins, serving a vital function in various metabolic processes. (6) Its normal value is from 70-120 micrograms per deciliter (µg/dL). (7) While the exact reasons for PCOS are not fully understood, some research has shown that trace elements may play a part in the occurrence of the illness. Several trace elements are crucial for proper metabolic activities, providing catalytic, structural, and regulatory functions via interacting with hormones, prohormones, and cellular receptors. (8) Zinc insufficiency in females can result in complications like impaired production and release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), abnormal ovary development, frequent miscarriages, prolonged pregnancy, birth defects, stillbirths, pre-eclampsia, toxaemia, and lower birth weights in infants. Oocytes exhibit most zinc transporters, metallothioneins, and metal regulatory transcription factors, suggesting a crucial role for zinc in maintaining genome integrity throughout early embryonic development. (9) Increasing data suggests that women with PCOS may be at a heightened risk for central nervous system and cardiovascular diseases. Many of these women have elevated levels of serum lipoprotein, blood glucose, and cholesterol, which heighten the likelihood of insulin resistance. Women with PCOS also have an increased likelihood of developing endometrial cancer. (10, 11)

PCOS may lead to depression, anxiety, and poor body image. Infertility, obesity, and undesirable hair growth might result in social stigma. This may impact all aspects of life, including family, relationships, work, and community engagement. (4) Aim of the study To assess if there is a significant relationship between serum zinc level and polycystic ovary syndrome.

Patients and method

A prospective case-control study was conducted in the gynecological department of Basrah Maternity and Children Hospital in Basrah City/Iraq during the period from 1st of October 2023 to 1st of September 2024. To assess if there is a significant relationship between serum zinc level and polycystic ovary syndrome. Women who visited the outpatient clinics of Basrah Maternity and Children Hospital during the study period were screened for PCOS. And divided into two groups: Group 1: fifty women who were diagnosed with PCOS. Women in this group were subdivided into two subgroups, Group 1a: twenty-five PCOS women with BMI ranged from 30.0-40.0. Group 1 b: twenty-five women with PCOS and BMI ranged from 18.5 to 29.9. Group 2: one hundred women who hadn't been diagnosed with PCOS. Women in this group are subdivided also into two subgroups. Group 2a: fourteen healthy control obese ladies with BMI ranging from 30.0 to 40.0. Group 2b: eighty-six healthy control women with BMI ranged from 18.5 to 29.9. Women suffering from acute or chronic diseases, such as Cushing syndrome and diabetes mellitus. Females in pregnancy, hypothyroid females. The use of any hormonal prescriptions, anti-diabetic and anti-obesity medications, insulin, or vitamin and mineral supplements, either currently or within the last two months, as well as those who are older than 45 and younger than 15 years old, were excluded from the study. Out of the 150 women who met the inclusion and exclusion criteria, 50 had a PCOS diagnosis based on the Rotterdam criteria, and 100 were chosen as the control group. These women were

from the outpatient clinic of Basrah Maternity and Children Hospital. This study has been approved by the Ethics Committee of the Faculty of Medicine at Basrah University. An informed consent was taken from each participating woman. And the Confidentiality of data was taken into consideration. A thoughtful questionnaire designed specifically for the study was used to gather data from the women who were included in the research. They were questioned regarding:
• Sociodemographic details including age, place of residence, employment, and marital status.

• Comprehensive PCOS medical history; The following PCOS symptoms and indicators were searched for: Inconsistency in the menstrual cycle, any increase in weight or incapacity to reduce weight, any excessive growth of hair on the body or face, any difficulty becoming pregnant or infertile, Oily skin and acne, and Any loss of hair.

• Clinical profile: a review of the surgical and medical histories of the women was conducted.

• Drug history: the use of hormonal medications received particular attention.

The following characteristics were checked for every woman:

• Anthropometric measurements include height, weight, and BMI, meaning kilos of weight divided by meters of height^2

• Blood samples were taken from all of the study participants and sent for serum zinc measurement (70 to 120 mcg/dL), FSH, and LH. Transabdominal/transvaginal ultrasonography was performed to show the presence of multiple peripheral ovary follicles each <10 mm, hyperechogenic theca, and increased ovary volume suggestive of PCOS. Data was entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 26 was used.

Results

The study includes 150 women, 50 women in the case group and 100 women in the control group. Their age ranges from 16 -42 years. Most of them were between 30-39 years. No significant statistical difference regarding the age since the p-value >0.05. Regarding the occupation, most of the women in both groups were housewives. More than half of women lived in urban areas. Regarding the BMI, there is a significant statistical difference between the case and control groups. Most of the women in the case group were obese while women in the control group were of normal weight. These data are presented in Table 1.

Table 1: the sociodemographic characteristics of the case and control group

variables		Case No. (%)	Control No. (%)	Total No. (%)	p-value
Age (16-42)	< 20	7 (36.8)	12 (63.2)	19 (100.0)	0.252
	20-29	17 (27.9)	44 (72.1)	61 (100.0)	
	30-39	23 (34.3)	44 (65.7)	67 (100.0)	
	≥ 40	3 (100.0)	0 (0.0)	3 (100.0)	
Occupation	Housewife	39 (33.9)	76 (66.1)	115(100.0)	0.784
	Employed	11 (31.4)	24 (68.6)	35 (100.0)	
Residency	Rural	21 (45.7)	25 (54.3)	46 (100.0)	0.633
	Urban	29 (27.9)	75 (72.1)	104 (100.0)	
BMI	18.5-24.9	10 (18.5)	44 (81.5)	54 (100.0)	0.001
	25-29.9	15 (26.3)	42 (73.7)	57 (100.0)	
	>30	25 (64.1)	14 (35.9)	39 (100.0)	
Total		50 (33.3)	100 (66.7)	150 (100.0)	

Table 2: The comparison between the case and control group

Variables	Case N=50 Mean ±SD	Control N=100 Mean ±SD	p-value
Zinc level	63.8 ± 20.6	76.8 ± 22.7	0.002
FSH	5.73 ± 1.56	4.63 ± 1.12	0.203
LH	7.51 ± 1.9	4.42 ± 0.9	0.031

Table 2 shows the comparison between the case and control group regarding the ZINC, FSH, and LH levels. The zinc levels were lower among women in the case group and this difference is of statistically significant p-value=0.002.

The FSH and LH levels both show higher means among PCOs, the LH shows significant differences between groups.

Table 3: Comparison between the obese PCO group and the obese control group

Variables	Obese PCO N=25 Mean ±SD	Obese control N=14 Mean ±SD	p-value
BMI	36.1± 4.3	34.9 ± 3.2	0.349
Zinc level	60.71 ± 3.01	71.2± 5.4	0.024
FSH	6.3 ± 1.5	4.21 ± 1.1	0.03
LH	10.87 ± 1.3	6.5 ± 0.82	0.003

The comparison between the obese women in both groups is presented in Table 3. There is a significant difference between obese women in the PCO group and women in the control group regarding zinc, FSH, and LH levels. The lower zinc mean was among PCO women, while a higher mean of FSH and LH was among the same group.

Table 4: Comparison between non-obese PCO group and non-obese control group

Variables	Non-obese PCO N=25 Mean ±SD	Non-obese healthy N= 86 Mean ±SD	p-value
BMI	23.6 ± 2.4	21.8 ± 3.5	0.255
Zinc level	75.3 ± 10.9	80.9± 5.9	0.065
FSH	5.2 ± 1.1	4.9 ± 0.8	0.321
LH	6.5 ± 2.9	6.08 ± 1.8	0.381

Table 4 shows a Comparison between the non-obese PCO group and the non-obese control group. A significantly lower level of zinc was noticed among non-obese women in the PCO group. No significant difference regarding the LH and FSH levels.

Table 5: Comparison between obese PCO group and non-obese PCO group

Variables	Obese PCO N=25 Mean ±SD	Non-obese PCO N=25 Mean ±SD	p-value
BMI	36.1± 4.3	23.6 ± 2.4	0.004
Zinc level	60.71 ± 3.01	75.3 ± 10.9	0.001
FSH	6.3 ± 1.5	4.2 ± 1.1	0.012
LH	10.87± 1.3	6.5 ± 2.9	0.014

Table 5 shows the Comparison between the obese PCO group and non-obese PCO group. There is a significant difference between the obese and non-obese women in the PCO group regarding the zinc, LH and FSH levels since the p-value < 0.05.

Table 6: Comparison between obese control group and non-obese control

Variables	Obese control N=14 Mean ±SD	Non-obese control N=86 Mean ±SD	p-value
BMI	34.9± 3.2	21.8 ± 3.5	0.002
Zinc level	71.2 ± 5.4	80.9± 5.9	0.038
FSH	4.21 ± 1.1	4.9 ± 0.8	0.223
LH	6.5 ± 0.82	6.08 ± 1.8	0.317

Table 6 shows a comparison between the obese control group and the non-obese control group. There's a significantly lower level of zinc among obese women in the control group. While no significant difference was noticed regarding the FSH and LH.

Discussion

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age, characterized by a variety of metabolic and reproductive abnormalities [(5)]. Understanding the sociodemographic and biochemical differences between women with PCOS and healthy controls is crucial for better management and treatment of this condition (12). This study aimed to compare several variables, including age, occupation, residency, body mass index (BMI), zinc levels, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) between women with PCOS and healthy controls.

The distribution of age, occupation, and residency between the PCOS and control groups did not exhibit significant differences in our study, likely due to effective matching between the groups.

In our study, BMI was notably higher in the PCOS group compared to healthy controls, with a significant p-value of 0.001. This finding is consistent with the established understanding that obesity is a common feature of PCOS as reported by

Zhang et al. (2023) [13] and this may contribute to its pathophysiology through mechanisms such as insulin resistance and hyperinsulinemia as mentioned by Diamanti-Kandarakis et al. (2012) [14]. In particular, 64.1% of women with PCOS had a BMI over 30, compared to only 35.9% in the control group, which further supports the association between higher BMI and PCOS and this is in line with what is reported by Barber et al. (2019) [15].

Zinc levels were significantly lower in women with PCOS compared to healthy controls ($p = 0.002$) in the current study. This is in line with some studies such as Dhar et al. (2024) [16]; and Kanafchian et al. (2018) [17] that suggest zinc deficiency may play a role in the oxidative stress and inflammation associated with PCOS. One possible mechanism for linking Zinc to PCOS can be through its effect on the insulin signalling system. Studies have indicated that in PCOS, insulin resistance stems from defects in insulin action beyond the receptor level with decreased zinc levels being associated with this insulin resistance [17]. The lower zinc levels observed in the current study, particularly among the obese PCOS subgroup ($p = 0.024$), may reflect dietary differences or altered zinc metabolism in obese individuals, which could exacerbate the symptoms of PCOS. A study by Fazel et al. (2022) [18] showed that organic zinc supplementation has beneficial effects on PCOS via decreased insulin resistance, restored the hormonal profile, and decreased the number of cysts in the ovaries. Jamilian et al. (2016) [17] conducted a randomized, placebo-controlled, double-blind study in women with PCOS and found that zinc supplementation significantly reduced hirsutism. Although this study found a significant beneficial effect of zinc supplementation on alopecia and hirsutism, no effect was observed on the hormonal profiles of women with PCOS.

In the current study, the FSH levels, though slightly higher in the PCOS group, did not differ significantly between the groups ($p = 0.203$). This is consistent with a previous study by Saadia (2020) [19], which often reports normal or slightly altered FSH levels in women with PCOS due to the condition's characteristic disrupted feedback mechanisms involving the hypothalamus and pituitary. However, this contradicts the findings of Al Kafhage et al., (2023) who found a significant increase in FSH levels in the PCOS group compared to the control group [20].

However, LH levels were significantly higher in the PCOS group compared to controls ($p = 0.031$), corroborating with the well-documented hypersecretion of LH in women with PCOS, which contributes to anovulation and hyperandrogenism and this is in line with Al Kafhage et al., (2023) [20] and Fattah et al. (2023) [21]. The difference in LH levels was even more pronounced in the obese PCOS subgroup ($p = 0.003$), suggesting that obesity may exacerbate LH dysregulation in PCOS patients, and this is in agreement with the findings of Shabbir et al. (2023) [22].

When comparing obese and non-obese individuals within the PCOS and control groups, the study found significant differences in BMI, zinc levels, FSH, and LH levels. Obese women with PCOS had significantly lower zinc levels and higher FSH and LH levels compared to their non-obese counterparts ($p < 0.05$ for all comparisons). These findings suggest that obesity may intensify the endocrine abnormalities seen in PCOS, potentially due to the added metabolic burden of excess adipose tissue. Similarly, in the control group, obese individuals also exhibited lower zinc levels compared to non-obese controls ($p = 0.038$), reinforcing the potential link between zinc deficiency and obesity, irrespective of PCOS status. These findings agree with Pokorska-Niewiada et al., (2022) [23].

The findings of these studies suggest that obesity exacerbates the hormonal imbalances associated with PCOS and that zinc deficiency may be a contributing factor.

Conclusions:

The findings indicate a significant association between reduced serum zinc levels and the presence of PCOS, particularly in obese women. This suggests that zinc deficiency may exacerbate the hormonal imbalances characteristic of PCOS, highlighting the importance of monitoring zinc status in managing this syndrome. Further research

is warranted to explore the therapeutic potential of zinc supplementation in women with PCOS.

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تقييم مستوى الزنك في مصل الدم لدى النساء المصابات بمتلازمة تكيس المبايض

الخلفية: متلازمة تكيس المبايض (PCOS) هي اضطراب غدد صماء وأيض شائع يؤثر على ٦-١٠٪ من النساء في سن الإنجاب. في حين أن الفيزيولوجيا المرضية للمتلازمة تظل معقدة، تشير الدراسات الحديثة إلى أن العناصر النادرة مثل الزنك قد تلعب دورًا مهمًا في تطورها وإدارتها.

الأهداف: هدفت هذه الدراسة إلى تقييم العلاقة بين مستويات الزنك في مصل الدم ووجود متلازمة تكيس المبايض بين النساء المراجعات لعيادات مستشفى البصرة للولادة والأطفال.

الطرق: أُجريت دراسة مقارنه للحالات والشواهد مستقبلية خلال الفترة من أكتوبر ٢٠٢٣ إلى سبتمبر ٢٠٢٤، شملت ١٥٠ امرأة: ٥٠ مصابة بمتلازمة تكيس المبايض و١٠٠ من الأصحاء. تم تصنيف المشاركات حسب مؤشر كتلة الجسم وتم قياس مستويات الزنك في مصل الدم. أُجريت التحليلات الإحصائية باستخدام برنامج SPSS النسخة ٢٦، مع استخدام اختبار كاي-تربيع للمتغيرات الفئوية واختبار t المستقل للمتغيرات المستمرة، واعتُبرت القيمة $p \leq 0.05$ ذات دلالة إحصائية.

النتائج:كشفت الدراسة عن انخفاض ملحوظ في مستويات الزنك في مصل الدم لدى النساء المصابات بمتلازمة تكيس المبايض مقارنةً بالمجموعة الضابطة (٦٣,٨ ± ٢٠,٦ ميكروغرام/ديسيلتر مقابل ٧٦,٨ ± ٢٢,٧ ميكروغرام/ديسيلتر، $p = 0.002$). في مجموعة متلازمة تكيس المبايض، كانت مستويات الزنك أقل بشكل واضح لدى النساء المصابات بالسمنة (٦٠,٧١ ± ٣,٠١ ميكروغرام/ديسيلتر مقابل ٧١,٢ ± ٥,٤ ميكروغرام/ديسيلتر في الضوابط المصابات بالسمنة، $p = 0.024$). بالإضافة إلى ذلك، لوحظت مستويات مرتفعة من هرمون اللوتين (LH) لدى النساء المصابات بالمتلازمة، وارتبطت بانخفاض مستويات الزنك.

الاستنتاجات: تشير النتائج إلى ارتباط كبير بين انخفاض مستويات الزنك في مصل الدم ووجود متلازمة تكيس المبايض، خاصةً لدى النساء المصابات بالسمنة. قد يشير ذلك إلى أن نقص الزنك يمكن أن يزيد من تفاقم الاختلالات الهرمونية التي تتميز بها هذه المتلازمة، مما يبرز أهمية مراقبة مستويات الزنك في إدارة المتلازمة.

الكلمات المفتاحية: تقييم، مصل الدم، مستوى الزنك، متلازمة تكيس المبايض.