Evaluation of Serum Zinc Levels in Patients with Poly Cystic Ovarian Syndrome (PCOS)

Ekhlas Faris Mohammad[1], Zamzam Nori Yassin[2], Zaid Kamel Mohsen[3]
[1]HD.G.O. Hit general hospital, ministry of health/ Iraq.
[2]HD.G.O. Alramadi teaching hospital for gynaecology and paediatric/ ministry of health/ Iraq.
[3]MSC. Microbiology/ Hit general hospital, ministry of health /Iraq.
Email: husrty@yahoo.com

Abstract
Background: Polycystic ovarian syndrome (PCOS) is a heterogeneous state that includes unovulation, increasing androgens hormones, and polycystic ovarian morphology. Women with PCOS have many reproductive and pregnancy-related complications, including a high risk of infertility, miscarriage, as well as a metabolic complication, for instance, excessive weight, insulin resistance, and type 2 diabetes mellitus. Over 300 enzymes, proteins, and transcriptional factors are regulated by trace elements, including zinc ions, the deficiency of it in the females can cause trouble such as a defect in the synthesis of gonadal hormones (follicular stimulating hormone and luteinizing hormone) and secretion, we aim to search whether there is any difference in the levels of serum zinc between the polycystic ovarian syndrome and healthy women. Material and method: The study was conducted in the private clinic from May 2021 till the end of August 2021. The study compared the levels of serum zinc between polycystic ovarian syndrome patients and healthy females. Seventy-two women have participated. Thirty-five women were diagnosed with polycystic ovarian syndrome and thirty-seven as controls. Results: Mean patients' weight, body mass index and waistline were considerably higher in the polycystic ovarian syndrome group ($p < 0.001$, $p = 0.008$ and $p < 0.001$ respectively). The levels of Serum zinc were significantly greater in the PCOS group (87.97 versus 65.27 µg/dl in the healthy group with p=0.002). There was significantly higher serum zinc in overweight PCOS patients (p=0.001). However, serum zinc and the body mass index have an insignificant negative correlation in PCOS and control groups. Conclusion: The levels of Serum zinc were higher in polycystic ovarian syndrome patients. Serum zinc level was not correlated with body mass index.
Keywords: Serum zinc, polycystic ovary syndrome (PCOS), infertility

1. Introduction

Polycystic ovarian syndrome (PCOS) is heterogeneous, including unovulation, rising androgens hormone, and polycystic ovarian morphology (1). The PCOS has been related to substantial reproductive and pregnancy difficulties, including a higher risk of infertility, miscarriage (2), as well as metabolic troubles, such as obesity, insulin resistance (I.R.), type 2diabetes Mellitus (3), dyslipidemia, and cardiovascular diseases (4,5). According to Previous reports, the percentage of obese or overweight women with PCOS are 40_50%, while 70% were reported to have insulin resistance (6, 7)

Although the specific causes of PCOS are unclear, some studies have suggested that trace elements have a role in the disease (8). Many trace elements are essential for optimal metabolic functions, having catalytic, structural, and regulatory functions interacting with hormones, prohormone, and cellular receptors (9). Inadequate supply of such nutrients causes functional impairment leading to various diseases. Trace elements also play an essential function in regulating the immune system and are needed for maintaining good body health (10).

Zinc is a crucial trace element necessary for the functions of over 300 proteins, enzymes, and transcriptional factors (11). The zinc ion plays a vital function in different physiological responses, involving oxidative stress and immunological function; it also helps to maintain the balance of hormones such as estrogen, progesterone, testosterone throughout the menstrual cycle (12); in addition to that, it is required for insulin synthesis, storage and structural integrity (13).

The total adult human body zinc status is about 1-3 g, with just about 0.1% of it being replenished daily (14). Zinc deficiency in women can cause ovarian dysfunction, recurrent abortion, pre-eclampsia, teratogenicity, stillbirth and low birth weight (15).

2. Materials and methods

The study was achieved to compare serum zinc between polycystic ovarian syndrome patients and healthy females from May 2021 through the end of August at a private clinic. Seventy-two women volunteers have participated. Thirty-five women presented with the polycystic ovarian syndrome (PCOS), and thirty-seven females were healthy controls.

The Rotterdam criteria are used to diagnose polycystic ovarian syndrome in women who meet two of the following three criteria (16):

1) Oligoovulation / Oligomenorrhea.
2) Clinical hyperandrogenism and/or biochemical

doi.org/10.31838/hiv23.02.193 Received: 27.10.22, Revised: 23.11.22, Accepted: 24.12.22.

hyperandrogenism.
3) Ultrasound examination shows polycystic ovaries.
The subjects' age was ranged from 18–45 years for patients and 20–45 years for control females. Women with hyper- and hypothyroidism, hyperprolactinemia, diabetes mellitus, mental, renal, liver, heart diseases and females taking zinc supplement for covid -19 were excluded.
The waist circumference was measured in inches by tape measure around the abdomen just above the patient's hipbones, Keeping the tape sung around the waist but not compressing the skin and after the patient breathes out. The body mass index was calculated by dividing the female weight in kilogram by the square of height in meters.
Three-hour postprandial venous blood samples (5 ml) were collected; then, the blood samples were transferred to a gel tube that clotted for 30 minutes at room temperature. The blood samples were centrifuged at 3500 rpm for 10 minutes. The serum obtained was kept at (-20°C) until used. Serum zinc was then measured by the colourimetric endpoint method at 578 nm wavelength.
The data were analyzed using Statistical Package for Social Sciences (SPSS) version 23.0. The descriptive statistics were measured, including frequency, mean, and standard deviation. The groups were compared by applying an independent sample t-test and analysis of variance (ANOVA). Pearson's correlation coefficient(r) was used to investigate the relationship between continuous variables, and when the p-value was less than 0.05, the results were regarded statistically significant.

The results

The data were given in mean plus-minus standard deviation. The mean patient's age in the PCOS group and control group was 25.94 ± 5.89 years and 27.81 ± 5.98 years, respectively, with no considerable variance between the two groups.Mean patients weight ,body mass index and waistline were considerably higher in PCOS group ($p < 0.001$, $p= 0.008$ and $p < 0.001$ respectively). Serum zinc levels were also significantly higher in the PCOS group (87.97 versus 65.27 µg/dl in the control group with p=0.002), as demonstrated in table 1 and figure 1.
In the PCOS group, 6 % were normally weighted, 34% overweighted, and 60% female were obese, while in the control group, 16% were normally weighted, 51% overweighted, and 33% were obese. Serum zinc levels in relation to the body weight for each group were insignificantly higher over-weight females (p=0.526) in the PCOS group and normal weighted females (p=0.169) in control, as illustrated in table 2. There was also significantly higher serum zinc in overweight PCOS patients (p=0.001) in the comparing with control group, as presented in table 3.

Table 1: Comparison of clinical parameters between PCOS and control groups

Parameters	PCOS group (Mean ± S.D.)	Control group (Mean ± S	.D.) p-value
Age (years)	25.94 ± 5.89	27.81 ± 5.98	0.186 Ŧ
Weight (kg)	80.17 ± 15.04	68.43 ± 10.89	< 0.001* Ŧ
Body mass index (Kg/m²)	31.95 ± 5.79	28.56 ± 4.67	0.008* Ŧ
Waist circumference (Inch)	37.57 ± 5.21	31.84 ± 3.91	< 0.001* Ŧ
Serum zinc level (µg/dl)	87.97 ± 39.31	65.27 ± 14.03	0.002* Ŧ

PCOS: Polycystic ovary syndrome; SD: Standard deviation;*: p-value less than 0.05; Ŧ: Independent t-test.

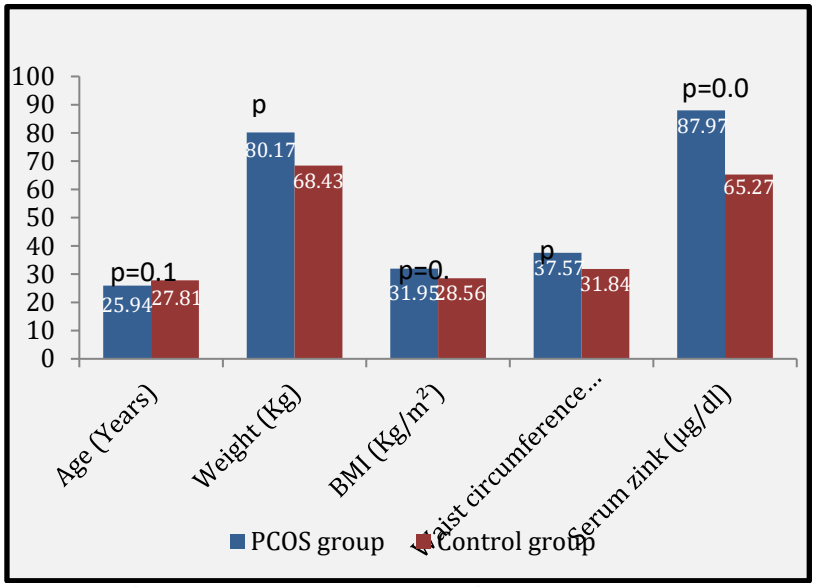

Figure 1: Comparison of serum zinc and demographic features between PCOS and control groups

Table 2: Comparison of serum zinc level between normal, overweight and obese females in PCOS and control groups				
Groups		Frequencies (n)	Serum zinc (µg/dl) (Mean ± S	D.) p-value
PCOS	Normal	2 (6%)	78.00 ± 41.01	0.526 ¥
	Overweight	12 (34%)	98.50 ± 31.10	
	Obese	21 (60%)	82.90 ± 43.68	
Control	Normal	6 (16%)	73.83 ± 8.04	0.169 ¥
	Overweight	19 (51%)	65.53 ± 16.47	
	Obese	12 (33%)	60.58 ± 10.34	
¥: ANOVA test				

Table 3: Comparison of serum zinc level between PCOS and control groups in normal, overweight and obese females			
Parameters	PCOS group (Mean ± S.D.)	Control group (Mean ± S	.D.) p-value
Normal	78.00 ± 41.01	73.83 ± 8.04	0.789 Ŧ
Overweight	98.50 ± 31.10	65.53 ± 16.47	0.001* Ŧ
Obese	82.90 ± 43.68	60.58 ± 10.34	0.093 Ŧ
*: p-value less than 0.05; Ŧ: Independent t-test.			

A substantial negative connection was also seen between serum zinc and waist circumference in the control group (r=-0.426, p=0.009); however, there was an insignificant negative correlation between serum zinc level with female's weight and body mass index in PCOS and control groups existent in table 4.

Table 4: Correlation between serum zinc with weight, BMI and waist circumference in PCOS and control groups				
Group		Weight	BMI	Waist circumference
PCOS	r	-0.160	-0.010	-0.159
	p value	0.358	0.957	0.363
Control	r	-0.177	-0.285	-0.426
	p value	0.294	0.087	0.009*
r: Pearson's correlation coefficient : *: p value less than 0.05.				

3. Discussion

Despite the fact that the aetiology of PCOS is unknown, it can be defined as a syndrome that emerges consequently the interplay of ecological and hereditary factors. In the pathophysiology of PCOS, the impact of insulin action, insulin secretion abnormality, gonadotropin alteration, and hereditary variables are all considered essential components (17,18).

Zinc is a well-known trace element required for many cellular functions. Zinc deficiency can cause various chronic illnesses since it is required in numerous metabolic processes such as glucose, protein, lipid, and nucleic acid synthesis and break down (19,20,21).

In this study serum, zinc levels in PCOS patients were substantially higher than in the control group (87.97 ± 39.31 versus 65.27 ± 14.03 and p=0.002).

Zinc levels in PCOS patients were shown to be greater than non-PCOS females in the study done by kurdaglu et al.; however, these values were limited in the reference range (66-110 microgram/dl) (22). In another study provided by Chakraborty et al., there was no significant disparity between the PCOS and control. Other studies by kanafchain et al. showed the statistically significant lower result in PCOS women than the control group (20,21).

As shown from the above data, serum zinc levels were found to be higher in the PCOS patient compared to control, and this may be related to the drugs used in the management of the PCOS like a multivitamin supplement, oral contraceptive pills, and metformin more than being a causative factor, because of all patients in our study sample have previous consultations in different medical clinics and had taken many medications.

In our study, 34% of patients were overweight, and 60% were obese. These results were in disagreement with Rajini et al., which demonstrated much lower overweight and obese percentages (28% and 21%, respectively). However, there is an agreement with the same study that serum zinc values were significantly higher in the PCOS group than in the control group (23).

Our current study shows that serum zinc levels were insignificantly higher in obese and normal-weighted PCOS patients but to a great extent higher in over-weighted PCOS patients compared to the healthy group; this result agreed with Mustafa et al., which demonstrated considerable higher serum zinc in obese PCOS and insignificantly higher serum zinc levels in normal-weighted PCOS females (24). Our study and Iqbal 2017 demonstrated subnormal

serum zinc levels in control females, indicating a significant public health issue; these findings agreed with Dhia et al., which demonstrated a high incidence of zinc deficiency in health control Iraqi individuals.

The present study also demonstrated no considerable relation between serum zinc levels and body mass index in both PCOS and control groups; these findings showed some inconsistency with Iqbal 2017, which showed a significant negative correlation in the control group with no significant relation between serum zinc and body mass index in PCOS group (25).

In conclusion, the levels of serum zinc were found greater in PCOS patients; however, the link between zinc status and PCOS patients was unclear; some studies demonstrated elevated serum zinc levels, others showed lower serum zinc levels, and this may be attributed to ethnic variations, dietary factors and multivitamin consumption and there was also subnormal serum zinc levels in the control group which may need further evaluation.

References

1. Krishnan A, Muthusamy S. Hormonal alterations in PCOS and its influence on bone metabolism. J Endocrinol. (2017)232: R99–113. DOI: 10.1530/JOE-16-0405

2. Palomba S, de Wilde MA, Falbo A, Koster MP, La Sala GB, Fauser BC.Pregnancy complications in women with polycystic ovary syndrome. Hum Reprod Update. (2015) 21:575–92. DOI: 10.1093/humupd/dmv029

3. OllilaMM, West S, Keinanen-Kiukaaniemi S, Jokelainen J, Auvinen J, Puukka K, et al. Overweight and obese but not normal-weight women with PCOS are at increased risk of Type 2 diabetes mellitus-a prospective population-based cohort study. Hum Rep. (2017) 32:423–31. DOI: 10.1093/humrep/dex030

4.S. Iftikhar, M. Collazo-Clavell, V.L. Roger, J.S. Sauver, R. Brown Jr., S. Cha,D. Rhodes, risk of cardiovascular events in patients with polycystic ovary syndrome,
Neth. J. Med. 70 (2) (2012) 74.

5. L.J. Moran, M.L. Misso, R.A. Wild, R.J. Norman, Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis, Hum. Reprod. Update 16 (4) (2010) 347–363.

6. H. Chun-Sen, W. Chien-Hua, C. Wan-Chun, L. Ching-Tzu, C. Chun-Jen, H. Ming-I, Obesity and insulin resistance in women with polycystic ovary syndrome, Gynecol.Endocrinol. 27 (5) (2011) 300–306.

7. K. Farrell, M.H. Antoni, Insulin resistance, obesity, inflammation, and depression in polycystic ovary syndrome: biobehavioral mechanisms and interventions, Fertil.Steril. 94 (5) (2010) 1565–1574.

8. Mehri Jamilian, Maryam Maktabi & Zatollah Asemi, (2017), A trial on the effects of magnesium-zinc-calcium-vitamin d co-supplementation on glycemic control and markers of cardio-metabolic risk in women with polycystic ovary syndrome. Arch Iran Med., 20(10), 640 – 645.

9. Mohammed Abbas Taher and Sarah Hashim Mhaibes. (2017). Assessment of some trace elements in obese and non-obese polycystic ovary syndrome (PCOS). International Journal of Science and Research, 6(9), 1333-1341.

10.Ciftci TU, Ciftci B, Yis O, Guney Y, Bilgihan A & Ogretensoy M. (2003). Changes in serum selenium, copper, zinc levels and Cu/Zn ratio in patients with pulmonary tuberculosis during therapy. Biol Trace Elem Res., 95(1), 65-71.

11. Prasad AS. Zinc: mechanisms of host defence. J Nutr. 2007; 137(5): 1345-9.

12. Environmental Health Criteria (EHC). Zinc. IPCS INCHEM. 2001; 221. Available at: http://www.inchem.org/documents/ehc/ehc/ehc221.htm

13. Maret W, Sandstead HH. Zinc requirements and the risks and benefits of zinc supplementation. J Trace Elem Med Biol. 2006; 20: 3-18. DOI: 10.1016/j.jtemb.2006.01.006.

14. Bedwal RS, Bahuguna A. Zinc, copper and selenium in reproduction. Experientia. 1994; 50: 626-40. DOI: 10.1007/BF01952862.

15.Y. P. Mamza, Z. B. Abdullahi, R. M. Gali, DS Mshelia, R. Y. Genesis & S. A. Habu. (2016). Status of Serum Zinc and Magnesium among Type 2 Diabetic Subjects in Maiduguri. IOSR Journal of Dental and Medical Sciences, 15(7), 66-70.

16. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19: 41-7. DOI: https://doi.org/10.1093/humrep/deh098.

17. Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism evisited. Endocrine reviews. 2016;37(5):467-520.

18. Evliyaoglu O. Polycystic ovary syndrome and hirsutism/Polikistik over sendromu ve hirsutism. J Turkish Pediatrics Archive. 2011: S97-S.

19. Cai L, Li X, Song Y, Cherian M. Essentiality and Toxicology of Zinc and Copper and its chelation therapy. Current Medicinal Chemistry. 2005;12.23:2753-63.

20. Kanafchian M, Mahjoub S, Esmaeilzadeh S, Rahsepar M, Mosapour A. Status of serum selenium and zinc in patients with polycystic ovary syndrome with and without insulin resistance. Middle East Fertility Society Journal. 2018;23(3):241-5.

21. Kulhan M, Kulhan NG, Nayki UA, Nayki C, Ata N, Ulug P, et al.Assessment of the relationship between serum vitamin (A, B 12, C, D, folate) and zinc levels and polycystic ovary syndrome. Archives of Medical Science-Civilization Diseases. 2017;2(1):62-9.

22. Kurdoglu Z, Kurdoglu M, Demir H, Sahin H. Serum trace elements and heavy metals in polycystic ovary syndrome. Human experimental toxicology. 2012;31(5):452-6.

23- Rajni, Smiti Nanda, Vandana Rani and Simmi Kharb Serum levels of zinc, copper and magnesium in polycystic ovarian syndrome: A cross-sectional study. International Journal of Clinical Obstetrics and Gynaecology 2020; 4(1): 88-91
24-Mustafa Bayraktar1 Ali Sami Gürbüz2 Bahadır Öztürk1 The Role of Irisin, Copper and Zinc Levelson Insulin Resistance in Polycystic OvarySyndrome Archives of Current Medical archives of Current Medical Research Arch Curr Med Res 2020; 1(1):12-19.
25- Iqbal G. Farhood.Assessment of Serum Zinc Level in Patients with Polycystic Ovary Syndrome.Iraqi JMS.2017; Vol.15(1):39-47.