

Evaluation of Zinc, Copper, Chromium and Thyroid Hormones levels in Serum of Iraqi Women with Polycystic Ovarian Syndrome

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Mohammed Asaad Mahdi

Department of Chemistry- College of Science- Diyala University

mohammed1979@sciences.uodiyala.edu.iq

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Abstract

Trace elements have an important function in the human body, where They play an role in the regulation and Stimulation of enzymatic reactions, metabolism, immunity and others. This study was conducted in the College of Science/Diyala University on women with polycystic ovarian syndrome (PCOS) from at Al-Batoul Hospital for childbirth/ Diyala. Thirty four women were diagnosed with polycystic ovarian syndrome (PCOS) based on Rotterdam 2003 criteria and were considered as patients groups. In contrast, seventeen healthy women with regular menstrual cycle and free of diseases were selected and considered as control group. Concentrations of trace elements (zinc, copper and chromium) were measured in the serum using an atomic absorption spectrophotometer in the Poisoning Consultation Center/ Medical City. The level of serum thyroid hormones [Thyroid Stimulating Hormone (TSH), Thyroxine (T4) and Triiodothyronine (T3)] was measured using the ELISA method. The results showed a significant decrease in the mean level of zinc in the PCOS group ($67.5 \pm 6.9 \mu\text{g/dL}$) compared with control group ($87 \pm 8.39 \mu\text{g/dL}$), ($p < 0.01$). The mean copper, Cu/Zn ratio and chromium level were significantly higher in the PCOS group (158.58 ± 8.3 , 2.38 ± 0.37 and $0.218 \pm 0.038 \mu\text{g/dL}$) respectively compared with control group (118 ± 9.5 , 1.37 ± 0.18 and $0.114 \pm 0.015 \mu\text{g/dL}$); ($P < 0.01$) respectively. There were no significant differences in the level of thyroid hormones between the two study groups.

Key words: zinc, chromium, copper, thyroid hormones, polycystic ovarian syndrome.

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تقدير مستوى الزنك، النحاس، الكروم والهورمونات الدرقية في مصول النساء العراقيات المصابات بمتلازمة التكيس المبيضي

محمد أسعد مهدي

قسم الكيمياء – كلية العلوم – جامعة ديالى

الخلاصة

تعتبر العناصر النزرة من الدوال المهمة في جسم الانسان. حيث تلعب دورا مهما في تنظيم وتحفيز التفاعلات الانزيمية، الايض، المناعة وغيرها. اجريت هذه الدراسة في كلية العلوم – جامعة ديالى على النساء المصابات بمتلازمة التكيس المبيضي في مستشفى البتول للولادة – ديالى. (34) من النساء تم تشخيصهن بمتلازمة التكيس المبيضي استنادا الى معيار روتردام 2003 وتم اعتبارهن كمجموعة مرضى. في المقابل، (17) امرأة سليمة منتظمة الدورة الحوضية وخالية من الامراض تم اختيارهن كمجموعة سيطرة. تراكيز العناصر النزرة (الزنك، النحاس والكروم) في مصل الدم تم قياسها باستخدام مطيافية الامتصاص الذري في مركز الاستشاري للسموم – مدينة الطب. مستوى هورمونات الدرقية في المصل (TSH, T4, T3) تم قياسها بطريقة ELISA . اظهرت النتائج انخفاضاً معنوياً في معدل مستوى الزنك لمجموعة المرضى ($67.5 \pm 6.9 \mu\text{g/dl}$) مقارنة مع مجموعة السيطرة ($87 \pm 8.39 \mu\text{g/dL}$) ، ($p < 0.01$) . معدل مستوى النحاس ، نسبة النحاس \ الزنك ومستوى الكروم كانت مرتفعة معنوياً لمجموعة المرضى (158.58 ± 8.3 , $2.38 \pm$) وعلى التوالي مقارنة مع مجموعة السيطرة (118 ± 9.5 , 1.37 ± 0.18 and 0.37 and $0.218 \pm .038 \mu\text{g/dL}$) على التوالي . لم يظهر أي اختلاف معنوي في مستوى الهورمونات الدرقية بين مجموعتي الدراسة .

كلمات مفتاحية: تقدير مستوى الزنك، الكروم، النحاس ، متلازمة التكيس المبيضي، هورمونات الدرقية.

Introduction

Polycystic ovarian syndrome (PCOS) Is the most important cause of female infertility and affects about (6 to 21%) of women of reproductive age^[1,2] It was also known as hyperandrogenism of clinical or biochemical associated with ovulatory dysfunction in the form of oligo-anovulation or polycystic ovary syndrome, presence of at least two of the above criteria with Rotterdam criteria^[3,4] The ovary is the female reproductive organ; there are two functions of the ovaries: synthesis of female sex hormones and the source of the oocyte^[5]. the

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mature and developing oocyte get within the environment provided by follicles^[6] these follicles are composed of different types and number of cells according to the stage of their maturation, and their size is indicative of the stage of oocyte development^[5,7], Symptoms of polycystic ovary syndrome include irregular or non-occurrence of menstrual cycles, dysfunction ovulation, decreased follicular maturation, pregnancy delay and insulin resistance.^[8,9] Endocrine disorders of ovarian polycystic syndrome with increased of androgens, normal levels of follicle stimulating hormone (FSH), hypersecretion of luteinizing hormone (LH) and elevated for ratio LH/FSH^[10], Other symptoms include weight gain, the growth of unwanted hair and acne with seborrhea.^[11]

Thyroid gland dysfunction leading to hypothyroidism is a common disorder affecting women more often than men. It can also be associated to primary hypothyroidism in some patients with PCOS. Thyroid disorder together with PCOS create independent risks of ovarian malfunction, could trigger alterations in ovulation, menstruation, endometrial receptivity, which consequently may have drastic influence on fertility.^[12,13]

Zinc is an important trace element that people required to stay healthy.^[14] Zinc plays a regulatory role and a stimulate in the cell, It is the first an intracellular ion^[15], activity of more than 300 different enzymes of various classes, supports healthy immune system, it plays a role in cell division, supports the healthy growth and development of the body during adolescence, childhood and pregnancy.^[14,16,17] Generally it can cause zinc deficiency growth retardation, diarrhea, delayed sexual maturation and impotence.^[18,19] In women deficient zinc levels may cause deterioration in oocytes and in severe cases causes' anovulation.^[20]

Copper is an essential trace element, it's play an important role in our metabolism, because it allows most critical enzymes to function properly.^[14] It's maintaining the strength of the blood vessels, also there is some of the essential roles copper plays in the body e.g. ATP synthesis, synthesis of the antioxidant superoxide dismutase which fights free radicals, keeps functioning normally for thyroid gland, contributes to the formation of certain hormones. The imbalances between zinc and copper levels play role in human health.^[21,22,23]

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Chromium is an essential element for insulin action. The effectiveness of insulin becomes unstable when chromium deficiency occurs, It is also necessary to metabolize carbohydrates, lipid and protein, also act as a cofactor for a many an important enzyme in the human body^[24,25]

The aim of the study was to assess the level of zinc, copper, chromium and hormones [Thyroid Stimulating Hormone (TSH), Thyroxine (T4) and Triiodothyronine (T3)] and the potential effect of these variables in women with PCOS compared to healthy women.

Material and Methods

This study was carried out in college science, Diyala University, between October 2016 and February 2017. The study included (51) female divided into two group, the first group (34) women patients with PCOS based on Rotterdam 2003 criteria. The second group consisted (17) healthy women volunteer that have normal menstrual cycle as control group. 5ml of venous blood samples from both groups were collected in a clean tube, after 15 minutes until complete blood clotting; the serum was separated using a centrifugation at 5000 rpm for 5 minutes. The serum was stored at -20°C in plain container until processing Serum levels of Thyroid Stimulating Hormone (TSH), Thyroxine (T4) and Triiodothyronine (T3) were measured by automated Enzyme-Linked Immunosorbent Assay (ELISA), in the laboratories of Al-Batoul Hospital for childbirth/Diyala, As for trace elements, zinc, copper and chromium were measured at the laboratories of Poisoning Consultation Center/ Medical City, using flame atomic absorption spectrophotometer.

Statistical analysis

All data were analyzed using the Statistical Package for Social Sciences (SPSS) computer program version 16. Data were expressed as (mean±SD) following analysis using independent samples t-test, which was performed for comparison between control and patients groups. A value of P less than 0.05 or 0.01 was considered significant.

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Results

After the diagnosis in Al-Batoul Hospital, (34) women were selected; their mean age was (23.92 ± 3.2 years) and considered as patients group, also, (17) women with a mean age of (25.4 ± 3.5 years) were also selected as a control group. After the statistical calculations of the clinical data, the following results were presented in Table (1):

Table 1: shows the mean (\pm SD) and the *P* value for the age and the level of trace elements in both groups

Parameter	Group	No.	Mean \pm SD	<i>P</i>
Age (years)	Control	17	25.40 \pm 3.5	<i>P</i> > 0.05
	Patients	34	23.92 \pm 3.2	
Zn (μ g /dl)	Control	17	87 \pm 8.39	<i>P</i> < 0.01
	Patients	34	67.5 \pm 6.9	
Cu (μ g/dl)	Control	17	118 \pm 9.5	<i>P</i> < 0.01
	Patients	34	158.58 \pm 8.3	
Ratio Cu / Zn	Control	17	1.37 \pm 0.18	<i>P</i> < 0.01
	Patients	34	2.38 \pm 0.37	
Cr (μ g/dl)	Control	17	0.114 \pm .015	<i>P</i> < 0.01
	Patients	34	0.218 \pm .038	

As shown in Table (1), the average age of the PCOS group was close to the mean age of the control group, with no significant differences between the two groups. The concentration of zinc in the PCOS group (67.5 ± 6.9) was less than the control group (87 ± 8.39) with a significant difference (*P* < 0.01). The results in Table (1) showed that the copper concentration and Cu / Zn ratio in the PCOS group (158.58 ± 8.3), (2.38 ± 0.37) were significantly higher than the control group (118 ± 9.5), (1.37 ± 0.18) respectively (*P* < 0.01), As for the concentration of the chromium element, it showed a significant increase in the PCOS group ($0.218 \pm .038$) compared with control group ($0.114 \pm .015$), (*P* < 0.01).

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Table 2: shows the mean (\pm SD) and the *P* value of the level of the thyroid hormones.

Parameter	Group	NO.	Mean \pm SD	<i>P</i>
TSH (μ U/ml)	Control	17	1.99 \pm 0.54	<i>P</i> > 0.05
	Patients	34	2.30 \pm 0.86	
T4 (nmol/L)	Control	17	141.16 \pm 35.47	<i>P</i> > 0.05
	Patients	34	120.12 \pm 24.7	
T3 (nmol/L)	Control	17	2.68 \pm 1.1	<i>P</i> > 0.05
	Patients	34	2.62 \pm 0.65	

The results in table (2) shows the level of TSH in the PCOS group (2.30 \pm 0.86) was close to the control group (1.99 \pm 0.54), (*P* > 0.05). As for the level of the hormone T4 in the PCOS group (120.12 \pm 24.7) it was lower in the control group (141.16 \pm 35.47), (*P* > 0.05). While the level of T3 hormone in the PCOS group (2.62 \pm 0.65) was very close to the control group hormone level (2.68 \pm 1.1), with no significant differences (*P* > 0.05).

Correlation

The results show the existence of a significant negative relationship between the ages of the PCOS group and the level of the hormone T4 (*r* = - 0.49, *P* = 0.045). One of the important relationships that has emerged in the results is a negative correlation between the concentration of zinc in PCOS group and the concentration of copper element, (*r* = - 0.622, *P* = 0.001).

Discussion

The study was conducted on women with polycystic ovary syndrome who suffer from infertility due to the non-continuity of growth and maturity of follicles and thus the anovulation. The study also attempted to establish the relationship or otherwise between polycystic ovarian syndrome and the level of measured elements and the effect of thyroid hormones (TSH, T4, T3) levels on PCOS. One of the results showed a significant decrease in the level of zinc for the PCOS group (*P* < 0.01) compared to the control group. This decrease in zinc level was identical to the results of previous researchers [26, 27, 28]. The results also showed a significant increase in the level of copper compared to the control group (*P* < 0.01). These results were close to the results of previous researchers [27, 29, 30], but they were opposing

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to the results of another study^[31]. The level of zinc has an important role in the human body through gender discrimination, female reproductive system, menstrual cycle, Ovulation process, fertilization, composition and maturation of sperm, at pregnancy, therefore zinc deficiency can cause several abnormal disorders including congenital anomalies, spontaneous abortion.^[32,33] And the imbalance in the level of zinc, whether in the decline or height might have significant effect on oocyte physiology^[34]. Other research has also pointed to a possible zinc deficiency that leads to weak production and secretion of FSH hormones, LH, abnormal ovarian growth.^[35] In 2007, a study of secondary infertility for women showed that zinc plays a role in sexual development, menstrual cycle and ovulation, Both folate and zinc have antioxidant properties that respond to reactive oxygen species (ROS).^[36] Zinc deficiency and high copper levels may be the cause of unexplained infertility, and therapeutic intervention to reverse this imbalance may be a cause of treatment.^[37] Copper contributes to the production of hemoglobin and contributes to metabolism because it allows many critical enzymes to function properly and maintain thyroid gland function.^[38,39] It also acts as a pro-oxidant and an antioxidant, therefore copper has a role in reducing the damage of free radicals that are generated naturally in the body by sweeping or neutralizing free radicals and thus reduce the damage of free radicals on the walls of cells.^[40, 41] Cu is found in Cu / Zn superoxide dismutase, an enzyme that removes the toxicity of superoxide by converting it into hydrogen peroxide and oxygen.^[42] The efficiency of an enzyme action(SOD) is due to a constant balance between the copper-zinc component. Therefore, when the copper-to-zinc ratio is disturbed, the ratio of harmful free radicals to the body will increase because of enzyme dysfunction, leading to significant damage to cell membranes and walls.^[38, 39] For our study, the copper-to-zinc ratio of the PCOS group was significantly higher than the control group. And perhaps this disorder in the proportion may have a key role in the disruption of ovarian function and lack of the persistence of maturity of follicle and growth of the formation of (dominant) and contrary to the decay of follicles, which leads to anovulation in polycystic ovarian syndrome.

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Chromium plays an important role in increasing the effectiveness of insulin.^[43] In the case of lack of chromium level causes a disturbance in the effectiveness of insulin, So it appeared Chromium supplements are given to women with type 2 diabetes, as well as for women with PCOS for the purpose of enhancing the effectiveness of insulin in the body and to regulate the level of glucose in the blood.^[44] Several studies have been conducted on chromium supplements given to women infected with PCOS and different doses. Many of the results were enhanced in increasing insulin resistance and adjusted for body mass. In some research, chromium supplementation regulates the menstrual cycle or stimulates ovulation, and in some of them have no effective results.^[45,46] The results in our study, the chromium level of the PCOS group was significantly higher than the control group ($P < 0.01$). It is contrary to the results of^[29,46]. Both the thyroid and ovaries are part of the endocrine system and belong to a common hormonal axis consisting of hypothalamus - pituitary – thyroid – ovaries. In previous studies on women with PCOS, thyroid disorders which is often associated with hypothyroidism or at risk of future hypothyroidism. The hypothyroidism may lead to a disturbance in the level of hormones (TSH, T4 and T3) and the reason was due to the hypothalamic-pituitary-ovarian disorders.^[12, 13, 47] For the current study, the results were not consistent with no significant difference between the level of the hormones (TSH, T4, T3) of the PCOS group compared to control group ($P > 0.05$), Which agree with the results of other researchers as well.^[48,49] which may link the PCOS with another factor such as insulin resistance^[50] or is a disturbance in the level of trace elements .

Conclusion

In conclusion, it is possible to conclude that the disturbance in the level of trace elements, zinc deficiency, copper elevation, and increased Cu / Zn ratio may play a role in PCOS and that the therapeutic intervention to modify these levels may be considered as a pathway for oocyte growth, maturity and ovulation.

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