EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 8
13-18
Year: 2017

ASSOCIATION BETWEEN POLY CYSTIC OVARIES SYNDROME AND SERUM LEVEL OF CHROMIUM, ZINC AND MAGNESIUM

Mosab Ismail Alazhari Ibrahim[1], Mariam Abass Ibrahim[2*], Sohaib Altieb Ibrahim[1], Haifa Awad Mustafa[1] and Altaf Suleman Mosad Taaha[2]

[1]Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences. Sudan International University – Sudan.
[2]Department of Clinical Chemistry, College of Medical Laboratory Science. Sudan University of Science and Technology – Sudan.

***Corresponding Author: Dr. Mariam Abass Ibrahim**
Department of Clinical Chemistry, College of Medical Laboratory Science. Sudan University of Science and Technology – Sudan.

Article Received on 23/05/2017 **Article Revised on 13/06/2017** **Article Accepted on 04/07/2017**

ABSTRACT

Background Polycystic ovary syndrome (PCOS), as the most prevalent endocrine disorder in reproductive-aged women, is associated with reproductive and metabolic abnormalities. Despite the large literature on the role of dietary composition in control of the metabolic disease, there is so little research on the mineral nutritional status of PCOS women. **Objectives:** The present study aimed to investigate serum levels of Chromium (Cr) zinc (Zn) and magnesium (Mg) in the patients with PCOS. **Materials and Methods:** This case-control study was carried out in Khartoum state, which included 40 PCOS women and 40 healthy subjects (both groups within age range of 19-52 years). Serum concentrations of Cr, Zn and Mg were estimated by flame atomic absorption spectrophotometer. **Results**: Subjects with PCOS showed significantly decreased serum concentrations of Cr, Zn and Mg as compared with the control group P.value 0.00, 0.00, 0.00 and mean ±SD 0.022 ± 0.008,0.14± 0.07, 0.21 ± 0.06, 0.53± 0.11 and 11.5 ± 2.3, 20.7± 3.7 respectively, with no statistically significant differences between chromium, zinc and magnesium and BMI group ≤ 25 and > 25 with P.value 0.26, 0.38, 0.9 mean ± SD 0.23 ± 0.008, 0.02 ± 0.008, 0.21± 0.05 ,0.23 ± 0.09 and 11.5 ± 2.5 ,11.5 ± 2.0 respectively. The results showed no statistically significant differences between chromium, zinc and magnesium and age group ≤ 35 and >35 years P. value 0.2 , 0.9, 0.2 mean ± SD 0.023 ± 0.008, 0.02± 0.008, 0.21± 0.050.21± 0.09 and 11.8± 2.5, 10.7± 1.38 respectively, results revealed that FSH level when compared with chromium, magnesium showed negatively insignificant correlation R: - 0.19 P-value: 0.2, R: - 0.18 P. value: 0.2 respectively, and positive insignificant correlation with Zinc, R: 0.2 P. value: 0.2. LH level showed no correlation with chromium with R: - 0.04 P. value: 0.7, and strong positive insignificant correlation with zinc R: 0.37 P. value: 0.01 and negatively insignificant correlation with magnesium R: - 0.13 P. value: 0.4. Prolactin level showed positively insignificant correlation with chromium R: 0.1 P.value: 0.5, magnesium R: 0.08 P.value: 0.6 and negatively insignificant correlation with zinc R: -0.22 P.value 0.16. **In Conclusions:** PCOS patient had deficiency in chromium, zinc and Magnesium levels.

KEY WORDS: PCOS, Zinc, Chromium, Magnesium, Trace elements, BMI, Sudan.

INTRODUCTION

Polycystic ovary syndrome is a common hormone disorder that affect women of reproductive age (4 - 10%)[1]. In each menstrual cycle, follicles grow on the ovaries, with in those follicles eggs develop, one of which will reach maturity faster than the others and be released into the fallopian tubes. this is known as ovulation. In the PCOS however, the ovaries are much larger than normal with series of undeveloped follicles that appear in clumps[2], These patients have steady state of relatively high estrogen, androgen, insulin resistance and LH levels rather than the fluctuating levels seen in ovulating women .Increased level of estrogen comes from obesity due to conversion of ovarian and adrenal androgen to estrone in body fat. High estrogen level suppresses FSH and causes relative increase in LH. Constant LH estimation of ovary result in anovulation, multiple cysts, and theca cell hyperplasia with excess androgen production (hyperandrogenism)[3], Many patients with PCOS are overweight and particularly in women with

both hyperandrogenism and anovulation, the condition is associated with metabolic syndrome of hyperinsulinaemia, insulin resistance and dyslipidemia that is recognize risk factor for development of both type2 diabetes mellitus and cardiovascular disease[4]. The polycystic ovary syndrome(PCOS) is a heterogeneous collection of signs and symptoms with disturbance of reproductive, endocrine and metabolic function[5], Chromium is an essential trace mineral required by the human body for normal carbohydrate and lipid metabolism[6] severe Chromium deficiency, characterized by impaired glucose tolerance, fasting hyperglycemia and eventually lipid disorders[7,8]. Research has demonstrated that chromium supplementation reduces glucose intolerance and relieves symptoms of type 1 and type 2 diabetes, as well as those of gestational diabetes[9]. The proposed mechanism of action for the insulin response to chromium is focused on the insulin receptor. Chromium activates the insulin receptor kinase and inhibits the insulin receptor phosphotyrosine phosphatase enzyme. This causes increased phosphorylation of the insulin receptor and increased insulin sensitivity and may facilitate glucose transport into cells[10]. In addition, chromium may augment insulin binding, insulin receptor number, and beta-cell sensitivity[11]. A study performed on women with PCOS showed that chromium supplementation improved glucose tolerance in this population[12]. Zinc is an essential trace element, critical for the function of over 300 enzymes including members of all enzyme classes and is closely involved in general metabolism of lipids, carbohydrates and proteins[13]. Zinc plays an important role in the synthesis, storage, secretion, conformational integrity of insulin monomers, and function of insulin. It is capable of modulating insulin action and improving hepatic binding of insulin[14]. Zinc is recognized as an integral component in a variety of glucose metabolism reactions and enhances glucose uptake into fibroblasts and adipocytes[15]. Disturbances of zinc homeostasis have been observed in diabetes and obesity[14, 16]. and also have been contributed to glucose intolerance, hyperglycemia and hypertriglyceridemia as well as dyslipidemia[17,18]. It has been reported that zinc deficiency is a risk factor of cardiomyopathy and myocardial infarction[19,20]. One of the possible mechanisms of zinc's relationship to PCOS other than insulin signaling system defects may be its effect on oxidative stress. Zinc is a potent antioxidant and its deficiency causes increased oxidative damage in multiple organs, including the heart[21]. No one exactly knows what causes PCOS Recent studies have indicated increased oxidative stress in the patients with PCOS [4, 6]. The importance of essential trace metals in health and disease is indisputable because of their vital role in specific concentration ranges and toxicity at relatively high levels. Essential trace elements have four major functions as being stabilizers, elements of structure, essential elements for hormonal function and cofactors in enzymes[7]. Zinc (Zn) is essential for the structure of many enzymes and plays a fundamental role in approximately 300 enzymatic reactions. It has a critical role especially in the function of metalloproteins, inducing members of oxidoreductase, hydrolase, ligase and lyase family and has coactivating functions with copper (Cu) in superoxide dismutase (SOD) or phospholipase C[8]. Magnesium (Mg) is the second most abundant intracellular cation found in the human body and is involved with over 300 ATP and kinase-dependent enzymatic reactions, including many of those involved in glucose metabolism, pancreatic insulin secretion, and insulin action in peripheral tissues[22]. Although dietary magnesium intake and renal excretion are important in maintaining magnesium homeostasis, its deficiency (including insufficient dietary intake) is associated with the presence of diabetes mellitus type 2 and other components of the metabolic syndrome including obesity, insulin resistance, hypertension, hyperlipidemia/dyslipidemia, and cardiovascular disease[23]. Magnesium (Mg) plays a major role in the regulation of glucose and insulin metabolism but conversely, insulin also affects serum Magnesium (Mg) concentrations. Given that hypomagnesaemia plays a putative role in the pathogenesis of insulin resistance and metabolic syndrome in the general population, it is intriguing to speculate that hypomagnesaemia may be encountered in younger PCOS patients who are insulin-resistant or have other manifestations of metabolic syndrome[24]. However, we aimed to investigate the levels of essential trace elements (Cr, Zn, and Mg).

MATERIALS AND METHODS

Study design: this was a descriptive case –control study. which was carried out in eighty subjects, 40 samples were taken from diagnosed PCOS patients, age (19 to 52 years old) and 40 apparently health females as control group, data were collected using questionnaire.

Study Area and Period: This study was conducted in Khartoum state, During the period from December 2016 to May 2017**.**

Study Population: A total of 80 subjects were enrolled in this study, 40 were diagnosed with poly cystic ovaries syndrome attended to Omdurman maternity hospital, Saudi maternity hospital, Banon fertility center, Alshifaa private center. and 40 were apparently healthy women served control group.

Inclusion and Exclusion criteria
All patientswere included, while patientsreceiving mineral and vitamins therapy or having disorder that may affect the level of element under study were excluded.

Ethical Consideration: The study had been approved by the local ethics committee of Sudan International University.

Informedconsentconsidering the aims of the study was given for participants, clinical information's and data were collected by questioner.

Sampling: venues blood specimen (5ml) was collected, samples kept in a test tube at room temperature then clotted blood sample were centrifuged at 4000 r.p.m for 10 min to obtain serum, samples were then stored at -20 C° till the time of analysis. The hormonal result was collected from paints record as clinical data.

Measurement of BMI: body mass index (BMI) was calculated by formula =weight (Kg) divided by height squared (m2).

Method of Estimation of Chromium, Zinc and Magnesium
Serum level of chromium, zinc and magnesium were measured using Atomic absorption spectrophotometer 210-VGP. according to the manufacture's protocol, serum chromium, zinc and magnesium were diluted 1:9, 1:5 and 1:5 with a 0.1% (w/v) lanthanum (as chloride) diluent, then diluted serum was aspirated and absorbance was measured at wave length 357.9 nm 213.9 nm and 285.2 nm[25] respectively. Control materials were included to insure accuracy of results.

Data Analysis: The Results were expressed as mean and SD. Independent t test was performed to evaluate and compare differences between the case and control group means. ANOVA test was performed to find the difference of chromium, zincand magnesium among age group in the study. Pearson's correlation coefficient was used to evaluate the relationship among the study variables (FSH, LH, Prolactin) and study parameter (Zn, Cr, Mg) P.value<0.05 were regarded statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows software (version 17.0).

RESLUTS
Result showed that level of chromium, zinc and magnesium in PCOS was significantly decreased compared to control group (Table 1). Results also showed that there were no statistically significant differences between chromium, zinc and magnesium and BMI groups ≤ 25 and >25 (Table 2), while results showed that there were no statistically significant differences between chromium, zinc and magnesium and age groups ≤ 35 and > 35 years (Table 3).Pearson correlation revealed that FSH level when compare with, chromium, magnesium showed negatively insignificant correlation, and positively insignificant correlation with Zinc. LH level with chromium showed no correlation, strong positively correlated with zinc level and negatively insignificant correlation with magnesium. And when compare level of prolactin showed positively insignificant correlation with chromium, magnesium. And negatively insignificant correlation with zinc (Table 4).

Table 1: Comparison of chromium, zinc and magnesium concentration instudy groups

Parameter	Case (Mean±SD)	control (Mean±SD)	P.value
Chromium 0.04-0.4 mg/l	0.022±0.008	0.14±0.07	0.00
Zinc 0.5-1.2 mg/l	0.21± 0.06	0.53± 0.11	0.00
Magnesium 17.0-28.0 mg/l	11.5±2.3	20.7±3.7	0.00

Table 2: Comparison of mean concentration of chromium, zinc and magnesium among BMI group ofpatients

Parameter	BMI≤ 25	BMI > 25	P.value
Chromium 0.04-0.4 mg/l	0.23± 0.008	0.02± 0.008	0.26
Zinc 0.5-1.2 mg/l	0.21 ±0.05	0.23± 0.09	0.38
Magnesium 17.0-28.0 mg/l	11.5 ±2.5	11.5 ±2.0	0.00

Table 3: Comparison of mean concentration of chromium, zinc and magnesium among Age groups of patients

Parameter	Age ≤ 35	Age > 35	P value
Chromium 0.04-0.4 mg/l	0.023± 0.008	0.02± 0.008	0.2
Zinc 0.5-1.2 mg/l	0.21± 0.05	0.21± 0.09	0.9
Magnesium 17.0-28.0 mg/l	11.5 ±2.5	10.7 ±1.38	0.2

Table 4: Correlation between chromium, zinc and magnesium and hormonal level of patients

Study parameter / Study variables	Chromium	Zinc	Magnesium
FSH			
R	0.19 -	0.2	0.18-
P.value	0.2	0.2	0.2
LH			
R	0.04-	0.37	0.3 -
P.value	0.7	0.01	0.4
Prolactin			
R	0.1	0.22 -	0.08
P.value	0.5	0.16	0.6

DISCUSSIONS

The polycystic ovary syndrome (PCOS) is a heterogeneous collection of signs and symptoms with disturbance of reproductive, endocrine and metabolic function[5]. The present study revealed that levels of chromium, zinc and magnesium were significantly decreased in PCOS patients compared to control group with P. value (0.00, 0.00, 0.00) respectively. This results were agreement with result of study done by Ismail et al[26]. WithP.value (0.00) for chromium andP.value (0.00) for zinc, and agreed with Guanchao Zheng et al[30], with P. value (0.009) for zinc, and in agreement with study result done by Yinhua Yu et al[27], with P.value (<0.05) for chromium, also This results were agreed with result of study done by Muneyyirci-Delaleet al[29], who reported significantly lower serum Mg 2+ and total magnesium in the PCOS patients compared with the controls. But the lowering levels of chromium, zinc and magnesium in this study were in Disagreement with study done by Kauffman et al[28], who reported significantly higher level of Zinc with P.value (<0.01) PCOS, and in disagreement with study done by Guanchao Zheng et al[30] who reported no statistical significance in chromium were observed between the patients and the control group .Also the results in disagreement with study of Kauffman et al[28] who denoted no significant difference of magnesium between PCOS patients and the controls with respect to its level which is in accordance with the results of our study. To the best of our knowledge, this is the first study investigated the serum levels of magnesium (Mg) in PCOS patients in Sudan, which is a multifactorial disease, and its exact cause remains a mystery. The current study results showed insignificant difference between chromium, zinc and magnesium and BMI groups of patients (≤ 25 and >25) with P. value (0.26, 0.38, 0.9) respectively. This finding in agreement with Ismail et al[26], who reported insignificant difference concerning chromium and zinc with P. value (0.347, 0.282) respectively. Also results revealed insignificant difference between chromium, zinc and magnesium and age groups of patients (≤ 35 and >35) with P.value (0.2, 0.9, 0.2,) respectively. which Disagreewith result of Ismail et al[25] who reported significant decreased in chromium with P.value (0.019). Regarding hormonal results of patients, FSH level when compared with chromium, magnesium showed negative insignificant correlation R (- 0.19) P. value (0.2) ,R (- 0.18) P. value (0.2)and positive insignificant correlation with Zinc R (0.2) P-value (0.2) respectively. LH level with chromium showed no correlation R (- 0.04) P. value (0.7), strong positively insignificant correlation with zinc level R (0.37) P. value (0.01), and negatively insignificant correlation with magnesium R (-0.13) P. value (0.4) respectively, while Prolactin showed positively insignificant correlation when compared with chromium, magnesium R (0.1) P.value (0.5), R (0.08) P.value (0.6) and negatively insignificant correlation with zinc R(- 0.22) P.value (0.16) respectively**.** This finding is support and in agreement with study of Yinhua Yu et al[27] with P.value (< 0.05) for Prolactin.

CONCLUSIONS

Development of women infertility was influenced by lower level of Chromium, zinc and Magnesium.

REFERENCES

1. Sozen I, Arici A. Hyperinsulinism and itsinteraction with hyperandrogenism in polycystic ovary syndrome ObstetGynecolSurv 2000; 55: 321-328.
2. Glenville M. MA, PhD, nutritionist specialising in women health, **Woman's health**, Issues. NHP.ORG April, 2009.
3. Inam.M, Danish, Medical diagnosis and management, 8th ed, 2006; 299-359.
4. Wild RA. Obesity, lipids, cardiovascular riskand androgen excess. Am J Med, 1995; 98: 27S32S.
5. Wilson BE, Gondy A. Effects of chromium supplementation on fasting insulin levels and lipid parameters in healthy, non-obese young subjects. Diabetes Research and Clinical Practice, 1995; 28: 179-184.
6. NidhiR :Padmalatha V, Prevalence of polycystic ovarian syndrome in Indian adolescents, 2011; Aug; 24(4): 223-230.7.
7. Goldhaber SB: Trace element risk assessment: essentiality vstoxicity.RegulToxicolPharmacol, 2003; 38: 232-242.
8. Wallach S: Clinical and biochemical aspects of chromium deficiency. J Am CollNutr, 1985; 4: 107- 120.
9. Cefalu WT, Hu FB. Role of chromium in human health and in diabetes. Diabetes Care, 2004; 27: 2741–2751.
10. Davis CM, Sumrall KH, Vincent JB. A biologically active form of chromium may activate a membrane phosphotyrosine phosphatase (PTP). Biochemistry, 1996; 35: 12963-12969.
11. Anderson RA. Nutritional factors influencing the glucose/insulin system: Chromium. J Am CollNutr, 1997; 16: 404-410.
12. Lucidi RS, Thyer AC, Easton CA, et al. Effect of chromium supplementation on insulin resistance and ovarian and menstrual cyclicity in women with polycystic ovary syndrome. FertilSteril, 2005; 84: 1755-1757.
13. TubeckS.Zinc supplementation or regulation of itshomeostasis: Advantages and Threats. BiolTraceElem Res., 2007; 119: 1-9.
14. Chausmer AB. Zinc, insulin and diabetes. J Am CollNutr, 1998; 17: 109-115.15. Coulston L, Dandona P. Insulin-like effect of zinc on adipocytes. Diabetes, 1980; 29: 665-667.
15. Di Martino G, Matera MG, De Martino B, Vacca C, Di Martino S, Rossi F. Relationship between zinc and obesity. J Med., 1993; 24: 177-183.
16. Bolkent S, Yanardag R, Bolkent S, Mutlu O, Yildirim S, Kangawa K. The effect of zinc supplementation on ghrelin-immunoreactive cells and lipid parameters in gastrointestinal tissue of streptozotocin-induced female diabetic rats. Mol Cell Biochem, 2006; 286: 77–85.
17. Kennedy M L, Failla ML. Zinc metabolism in genetically obese (ob/ob) mice. J Nutr, 1987; 117: 886-893.
18. Singh RB, Niaz MA, Rastogi SS, Bajaj S, Gaoli Z, Shoumin Z. Current zinc intake and risk of diabetes and coronary artery disease and factors associated with insulin resistance in rural and urban populations of North India. J Am CollNutr, 1998; 17: 564–570.
19. Singh RB, Niaz MA, Rastogi SS, Bajaj S, Gaoli Z, Shoumin Z. Current zinc intake and risk of diabetes and coronary artery disease and factors associated with insulin resistance in rural and urban populations of North India. J Am CollNutr, 1998; 17: 564–570.
20. Soinio M, Marniemi J, Laakso M, Pyorala K, Lehto S, Ronnemaa T. Serum zinc level and coronary heart disease events in patients with type 2 diabetes. Diabetes Care, 2007; 30: 523–528.
21. Guler I. Zinc and Homocysteine Levels in Polycystic Ovarian Syndrome Patients with Insulin Resistance. Biol Trace Elem Res., 2014.
22. Saris N, Mervaala E, Karppanen H, Khawaya J, LewenstamAMagnesium: an update on physiological, clinical, and analytical analysis. ClinChemActa. 2000; 294: 1–26. .
23. Fung TT, Manson JE, Solomon CG, Liu S, Willett WC, HuFB. The association between magnesium intake and fastinginsulin concentration in healthy middle-aged women. J AmCollNutr. 2003; 22: 533–8.
24. Guzick D. Polycystic ovary syndrome. ObstetGynecol 2004; 103: 181–93.
25. BUCK SCIENTIFIC 210/211 VGP, OPERATOR MANUAL, JANUARY 2003; 154 – 176.
26. Ismail et al, Rehab Ibrahim Badawi, Omer FadulIdres, ASSESSMENT OF CHROMIUM AND ZINC LEVEL AMONG POLYCYSTIC OVARYSYNDROME PATIENTS ,European Journal of Biomedical AND Pharmaceutical sciences, 2016; (3): 27-30.
27. Yinhua Yu et al ,Nirvana Samy,AnnaBenrick ,LiudmilaIvanova, Some Altered Trace Elements in Patients with Polycystic Ovary Syndrome,British Journal of Medicine & Medical Research, 2017; 20(3): 1-10, Article no.BJMMR.31503.
28. Kauffman RP, Tullar PE, Nipp RD, Castracane VD. Serum magnesium concentrations and metabolic variables in polycystic ovary syndrome. Acta Obstetritciaet Gynecology Scandinavia. 2011; 90: 452–458.
29. Muneyyirci-Delale O, Nacharaju VL, Dalloul M, Jalou S, Rahman M, Altura BM. Divalent cations in women with PCOS: implications for

cardiovascular disease. GynecolEndocrinol 2001; 15: 198–201.

30. Guanchao Zheng et al, Lijun Wang, ZhizhunGuo, Lingbin Sun, Lingling Wang, Chonggang Wang, ZhenghongZuo, HuilingQiu, association of serum heavy metals and trace element concentrations with reproductive hormone levels and polycystic ovary syndrome in a chinese population, 2014 /Accepted: 2 March 2015, Springer Science+Business Media New York 2015.