

The Association between Serum Zinc Levels and Insulin Resistance among Polycystic Ovary Syndrome Patients in Duhok City, Kurdistan Region, Iraq

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a relatively common endocrine and metabolic problem. Patients with PCOS are known to have a higher incidence of insulin resistance. The homeostasis model assessment (HOMA) is an indirect, rapid, accurate, and cost-effective method of assessing insulin resistance based on patient's fasting plasma insulin and glucose concentrations. Several studies have reported a significant correlation between HOMA and the traditional hyperinsulinemic-euglycemic clamp method. Zinc deficiency promotes insulin resistance, and that zinc supplementation can prevent or, at least, alleviate insulin resistance in selected patient populations. **Objective:** The current study primarily aims at defining the association between insulin resistance and zinc deficiency among both PCOS and selected controls. It also looks at certain risk factors associated with obesity among the study population in Duhok City, Kurdistan Region, Iraq. **Materials and Methods:** The current case-control study was performed at Azadi Teaching Hospital/Gynecological Outpatient Clinic in Duhok City/Kurdistan Region/Iraq. The study included 80 women (40 cases with PCOS and 40 controls of healthy women). **Results:** There was no age difference between both groups (Mean = 26.77 years, standard deviation [SD] = 6.42 years for PCOS cases versus mean and SD of 27.57 years and 6.45 years, respectively; $P = 0.48$). Likewise, there was no difference in the serum zinc levels between cases and controls. However, patients with PCOS had significantly higher Body mass index and HOMA scores compared to the controls ($P = 0.005$ and 0.007 , respectively). **Conclusion:** Higher serum zinc levels are independently associated with lower HOMA. Patients with PCOS had significantly higher insulin resistance when compared to the controls of similar age and zinc level.

Keywords: Insulin resistance, Kurdistan region, polycystic ovary syndrome patients, serum zinc levels

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a relatively common endocrine and metabolic problem.^[1] About 4%–12% of women in the reproductive age suffer from this disease, putting them at risk of various fertility and cardiometabolic complications.^[2–4] Patients with PCOS are known to have a higher incidence of insulin resistance, dyslipidemia, hypertension, and obesity.^[5,6]

The homeostasis model assessment (HOMA) is an indirect, rapid, accurate, and cost-effective method of assessing insulin resistance based on patient's fasting plasma insulin and glucose concentrations. Several studies have reported a significant correlation between HOMA and the traditional hyperinsulinemic-euglycemic clamp method.^[7–9] Owing to its

robustness, HOMA is the most commonly used measure of insulin resistance in epidemiological studies.^[10]

Several studies have recently shown that zinc deficiency promotes insulin resistance and that zinc supplementation can prevent or, at least, alleviate insulin resistance in selected patient populations.^[11–13] This essential element is required for the proper function of over 300 enzymes and 2,000 transcription factors.^[14] It can activate the insulin signaling pathway through inhibiting the function of protein tyrosine

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phosphatase with resultant increased phosphorylation and activation of the insulin receptor.^[15] Moreover, zinc can promote glucose transport through translocating glucose transporter 4 to the surface membrane, thereby exerting an insulin mimetic effect.^[16,17]

The current study primarily aims at defining the association between insulin resistance and zinc deficiency among both PCOS and selected control patients. It also looks at certain risk factors associated with obesity among the study population in Duhok City, Kurdistan Region, Iraq.

MATERIALS AND METHODS

Study design and sampling

The current case–control study was performed at Azadi Teaching Hospital/Gynecological Outpatient Clinic in Duhok City/Kurdistan Region/Iraq. The study included 80 women (40 cases with PCOS and 40 controls of healthy women who accompanied the PCOS cases). The recruitment period extended from August 2017 to March 2018.

Inclusion criteria

Inclusion criteria for the current study were as follows: patients with a diagnosis of PCOS according to the Rotterdam criteria requiring at least two out of the three following characteristics: (i) cycle disorder, (ii) clinical or biological hyperandrogenism, and (iii) antral follicular excess on ultrasound with ≥ 12 follicles from 2 to 9 mm per ovary and/or ovarian volume ≥ 10 ml.^[18]

Ethical considerations

This study was approved by the Kurdistan Board for Medical Specialties/Directorate of Training Affairs/Scientific Research Units. A written informed consent was obtained from each participant.

Statistical analysis

Two independent samples *t*-test was used to calculate the *P* values of the difference in mean of age, serum zinc, body mass index (BMI), and HOMA scores between cases and controls. Fisher's exact test was used to calculate the *P* value of the association between marital and PCOS statuses, as well as the *P* value of the association between marital status and BMI. Multiple binary logistic regression analysis was used to calculate the adjusted odds ratios (ORs), 95% confidence intervals (CIs) and *P* values for the association of selected covariates (age, PCOS status, and serum zinc) with the outcome variable of "HOMA score." PCOS status was used as a categorical variable while both age and serum zinc were used as continuous ones. Likewise, multiple binary logistic regression analysis was used to calculate the adjusted ORs, 95% CIs and *P* values for the association of age, PCOS status, and marital status with the outcome variable of "BMI." The latter was categorized to "<25" and "25 and more." The age was used as a continuous variable in the model.

Hosmer–Lemeshow test was used to check for goodness-of-fit of the regression models. All statistical analyses were performed

using Statistical Package for the Social Sciences version 18 for Windows/MAC. (SPSS, IBM Company, Chicago, USA). All tests were two-sided with 0.05 level of significance.

RESULTS

A total of 80 participants were incorporated in the current study, of whom 40 participants had PCOS diagnosis and 40 participants served as controls. There was no age difference between both groups (Mean = 26.77 years, standard deviation [SD] = 6.42 years for PCOS cases versus mean and SD of 27.57 years and 6.45 years, respectively; *P* = 0.48). Likewise, there was no difference in the serum zinc levels between cases and controls. However, patients with PCOS had significantly higher BMIs and HOMA scores compared to the controls (*P* = 0.005 and 0.007, respectively) [Table 1].

Figure 1 shows that there is no difference between cases and controls in terms of the marital status (*P* = 0.81).

When adjusted for age and PCOS status, patient with higher serum zinc levels had significantly lower HOMA scores (OR = 0.93, 95% CI = 0.91–0.97, *P* = 0.01). On the other hand, patients with PCOS had significantly higher HOMA scores compared to controls of similar age and serum zinc levels (OR = 3.9, 95% CI = 1.21–12.66, *P* = 0.02). Likewise, higher HOMA scores were observed with older

Table 1: Characteristics of polycystic ovary syndrome cases and controls

Variables	Mean $\pm$ SD		<i>P</i>
	Cases	Controls	
Age (years)	26.77 (6.62)	27.57 (6.45)	0.48
Serum zinc (mg/dl)	107.44 (27.69)	93.34 (23.25)	0.16
BMI (kg/m ²)	27.18 (5.55)	24.18 (3.21)	0.005
HOMA	3.58 (1.09)	2.99 (0.99)	0.007

BMI: Body mass index, HOMA: Homeostasis model assessment, SD: Standard deviation

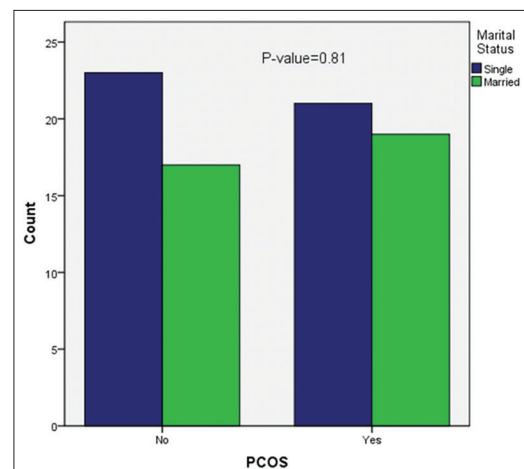


Figure 1: Difference between cases and controls in the marital status

ages even after controlling for PCOS status and serum zinc levels (OR = 1.10, 95% CI = 1.05–1.18, $P = 0.03$) [Table 2].

Figure 2 shows that married participants had a significantly higher BMI ($P = 0.006$). However, this association is confounded by age and PCOS status as shown in Table 3. On the other hand, older ages and patients with PCOS had significantly higher BMIs in the multivariate analysis ($P = 0.04$ and 0.01, respectively).

Table 2: Multiple binary logistic regression model of the homeostasis model assessment scores associated with the variables of polycystic ovary syndrome status, age, and serum zinc levels

Variables	OR	95% CI	P
PCOS			
No	1	1.21-12.66	0.02
Yes	3.9		
Age	1.10	1.05-1.18	0.03
Serum zinc	0.93	0.91-0.97	0.01

PCOS: Polycystic ovary syndrome, OR: Odds ratio, CI: Confidence interval

Table 3: Multiple binary logistic regression model of the body mass index associated with the variables of polycystic ovary syndrome status, age, and marital status

Variables	OR	95% CI	P
PCOS			
No	1	1.231-9.31	0.01
Yes	3.39		
Age (years)			0.04
<30	1	1.10-11.45	
30 and above	3.42		
Marital status			0.21
Single	1	0.66-6.35	
Married	2.05		

PCOS: Polycystic ovary syndrome, OR: Odds ratio, CI: Confidence interval

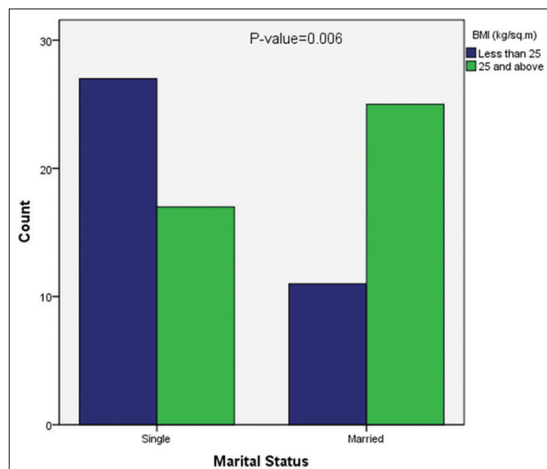


Figure 2: Difference between single and married participants in terms of the body mass index

DISCUSSION

To the best of our knowledge, this is the first study that analyzes the association between serum zinc levels and insulin resistance in Kurdistan Region of Iraq. Higher serum zinc levels are independently associated with lower HOMA (and less insulin resistance). This finding is compatible with the results of a recent clinical trial conducted in Iran, which showed that magnesium-zinc-calcium-vitamin D co-supplementation for 12 weeks among patients with PCOS had beneficial effects on insulin metabolism and markers of cardiometabolic risk.^[19] Similar results have been replicated in other studies that showed zinc supplementation has a beneficial effect on insulin resistance as measured by HOMA index and lipid profile in PCOS women, and that a disturbance in zinc homeostasis underlies some of the deleterious effects of insulin resistance among patients with type 2 diabetes mellitus.^[11,17,20-22]

As expected, patients with PCOS had significantly higher insulin resistance when compared to the controls of similar age and zinc level. This is compatible with the known metabolic effects of PCOS on insulin receptor sensitivity and glucose tolerance.^[23] Older age was also an independent risk factor for insulin resistance in our study, as indicated by higher HOMA scores associated with older ages. Chronic, low-grade, and systemic inflammation have been incriminated in the pathogenesis of aging and its related diseases, including diabetes mellitus.^[24] It has been shown that such inflammatory status is implicated in the process of adipose tissue deposition and that adipogenesis is by itself associated with increased levels of pro-inflammatory cytokines that interfere with insulin signaling.^[25,26]

Studies have shown that marriage is linked to lower body weights, whereas divorced and widowed people have heavier body weights.^[27-30] However, the association between body weight and marital status is subject to considerable cultural variations. Although married people were shown to weigh more in the univariate analysis of our study participants, such an association did not exist when we adjusted for age and PCOS status in the multivariate analysis. This indicates the marital status was a confounder, rather than a risk factor for obesity, in our study.

Our study has certain limitations, including the small sample size and relatively small number of variables taken into consideration. However, it does provide an insight about the association of serum zinc with HOMA in PCOS patient, and perhaps in the general population. Besides, it is the first study that deals with such an analysis in the Kurdistan Region of Iraq. However, larger studies need to be done to evaluate the effect of such an association at a larger population scale. Interventional studies with zinc supplementation for patients with insulin resistance can be considered.

CONCLUSION

From results of this study, we can conclude that higher

serum zinc levels are independently associated with lower HOMA. Patients with PCOS had significantly higher insulin resistance when compared to the controls of similar age and zinc level.

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Conflicts of interest

There are no conflicts of interest.

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