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The Association between Zinc and Copper and Cardiometabolic Risk Factors in Adults

Dana Alkudsi[1], Sara Hamad[1], Hanan Alkeldi[1]
Supervised by: Dr. Abdelhamid Kerkadi[1], Dr. Abdelali Agouni[2], Ms. Reem Salih[1]

[1]Human Nutrition Department, College of Health Sciences, Qatar University, Doha, Qatar
[2]Pharmaceutical Sciences Department, College of Pharmacy, Qatar University, Doha, Qatar

ABSTRACT

Cardiometabolic risk (CMR) factors increase the likelihood of developing cardiovascular diseases (CVD). In Qatar, 24% of the total deaths are attributed to CVDs. Several nutritional disturbances have been linked to high risk of CVD. Many studies have discussed the effects of zinc (Zn) and copper (Cu) on CMR factors; however, evidence has been controversial. This investigated the association between CMR factors and the status of Zn, Cu, and Zn/Cu ratio. A total of 575 Qatari adults (≥18 years) were obtained from Qatar Biobank. Plasma levels of Zn and Cu were determined using inductively coupled plasma mass spectrometry (ICP-MS). Anthropometric data and CMR factors were determined using standard methods. Adjusted associations between minerals and CMR were estimated by logistic regression. The associations' strength was tested using partial correlation. Zn was not strongly correlated (p-value>0.01) or significantly associated with CMR factors and metabolic syndrome (MetS). Cu levels correlated positively with body mass index (BMI) (0.23; p<0.001), pulse rate (PR) (0.18; p<0.001), total cholesterol (0.13; p=0.01), and high-density lipoproteins (HDL) (0.27; p<0.001); and negatively with diastolic blood pressure (DBP) (−0.13; p=0.01). High Cu significantly decreased the risk of MetS (0.121; p<0.001). Furthermore, Zn/Cu ratio positively correlated with waist circumference (0.13; p=0.01), systolic blood pressure (0.13; p<0.01), and DBP (0.14; p<0.01); and negatively with BMI (−0.19; p<0.001), PR (−0.17; p<0.001), and HDL (−0.27; p<0.001). High Zn/Cu ratio increased the prevalence of low HDL (4.508; p<0.001) and MetS (5.570; p<0.01). These findings suggest that high Cu levels are associated with a protective effect on DBP, HDL and MetS and that high plasma Zn/Cu ratio is associated with the risk of low HDL and MetS. We recommend future studies to focus on minerals status among abdominally obese and prediabetic subjects because of the probable link between low serum Zn and Cu and insulin resistance and CVD.

INTRODUCTION

- CMR factors are factors that increase the likelihood of developing cardiovascular events.
- Zn is a heavy metal known to suppress inflammation, reduce oxidative stress, and catalyze lipid metabolic enzymes. It is also used by muscle and fat cells to metabolize glucose and regulate insulin receptors synthesis. Moreover, Zn has a role in controlling blood pressure and vascular tune modulation.
- Cu is an essential cofactor in numerous antioxidant and oxidoreductive enzymes which reduce atherosclerosis and inflammation and improve cardiovascular function and fat metabolism. Cu indirectly affects diabetes and blood pressure regulation.
- Many studies discussed the association between Zn, Cu and CMR factors. In highlight of lipid profile, Zn relationship to lipid profile indicators is controversial[1,2]. On the other hand, plasma Cu was positively associated with high TC, HDL, and risk of dyslipidemia[3]. In addition, an inverse relationship was found between Cu:Zn ratio and lipid profile ratios[1].
- Zn relationship with diabetes is not well established. HbA1c was found to be positively associated with plasma concentration of Cu and negatively with Zn:Cu ratio in type 2 diabetes[4]. Further, Cu and Zn intakes and Cu:Zn ratio had no association with HTN[5,6]. However, a study showed that high Cu levels may elevate the susceptibility of HTN[7].

METHODOLOGY

Initial sample size= 575
Final sample size= 437

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1. Adult men and women aged ≥18 years old
2. Qatari and residents, who have lived for ≥15 years in Qatar
3. Fasting participants with data on Zn, Cu, and CMR factors (WC, BMI, lipid profile data, glucose, insulin, Hb1Ac, SBP, DBP, and PR)
4. Excluded: 1- diagnosed with diabetes, CVD, and HTN; 2- taking mineral supplements or medications; 3- having pacemakers; 4- pregnant or lactating women

Wall mounted stadiometer with no shoes on

Calibrated scale with light clothes

Measured at the level of the umbilicus using a non-stretchable tape

TG to glucose ratio was calculated using a formula

Friedewald formula was used to calculate LDL

Fasting glucose, HbA1c, insulin, HDL, TC, and TG were determined using standard methods

BP: average of 3 mercury sphygmomanometer measurements
PR: standard method

HOMA-IR was calculated using fasting glucose

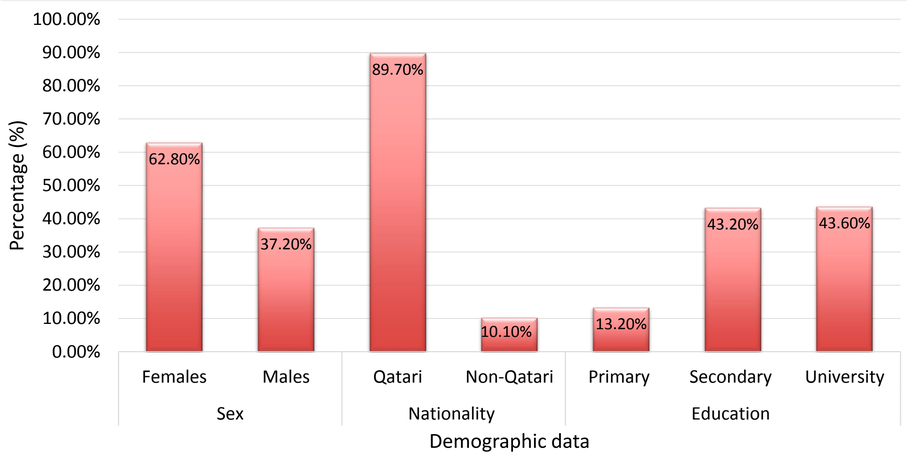
Zn Cu — Inductively coupled plasma mass spectrometry (ICP-MS)

SPSS 26

Multiple linear regression was performed to determine the relationship between mineral indicators and CMR	Odds ratio and 95% confidence intervals were determined	The regression model was adjusted for gender, age, BMI, and physical activity	Partial correlation to elucidate the association between trace minerals and CMR factors	MetS: 3/5 of the following: hyperglycemia or on DM treatment, high BP or on HTN drugs , high TG, low HDL, and central obesity

RESULTS

Figure 1: Demographics of the study population



The mean age of the 437 participants was 41±12.6 years. The mean serum zinc and copper levels were 12.6±2.0 and 18.2±4.7 µmol/L, respectively.

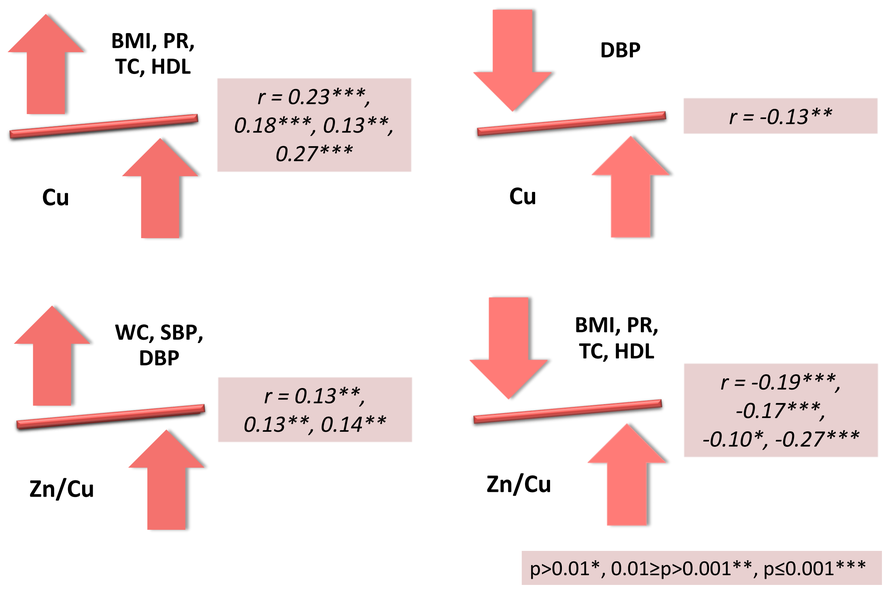
Table 1: Comparison of cardiometabolic markers according to serum Zn, Cu, and Zn to Cu ratio[1]

	Zinc tertiles			Copper tertiles			Zn to Cu ratio tertiles		
	T1: <11.6 µmol/L	T2: 11.6-13.3 µmol/L	T3: >13.3 µmol/L	T1: <15.8 µmol/L	T2: 15.8-19.1 µmol/L	T3: >19.1 µmol/L	T1: <0.63	T2: 0.63-0.79	T3: >0.79
Cardiometabolic markers[2,3]									
PR (bpm)	71.3 (10.6)	70.3 (9.6)	69.7 (10.1)	**68.7 (10.2)**	**71.1 (9.8)**	**71.5 (10.2)***	71.7 (10.7)	70.8 (8.9)	68.9 (10.5)
TC (mmol/L)	4.8 (0.9)	5.1 (1.1)	5.0 (1.0)	**4.8 (1.0)**	**5.1 (1.1)**	**5.1 (1.0)****	**5.0 (0.9)**	**5.1 (1.1)**	**4.8 (1.0)***
HDL (mmol/L)	1.5 (0.4)	1.4 (0.4)	1.4 (0.4)	**1.3 (0.3)**	**1.4 (0.4)**	**1.5 (0.4)*****	**1.5 (0.4)**	**1.4 (0.4)**	**1.3 (0.4)*****
TG (mmol/L)	**1.1 (0.6)**	**1.4 (1.4)**	**1.3 (0.6)***	1.2 (0.6)	1.3 (1.2)	1.3 (0.8)	**1.2 (0.6)**	**1.4 (1.4)**	**1.2 (0.6)***
HbA1c (%)	5.6 (1.2)	5.7 (1.2)	5.8 (1.2)	**5.4 (0.8)**	**5.8 (1.3)**	**5.9 (1.4)*****	5.8 (1.3)	5.8 (1.2)	5.5 (1.1)
TyG	**4.5 (0.3)**	**4.6 (0.4)**	**4.6 (0.3)***	4.6 (0.3)	4.6 (0.3)	4.6 (0.3)	4.6 (0.3)	4.6 (0.4)	4.6 (0.3)

[1] Results are expressed as Mean (SD).
[2] PR= pulse rate; TC= total cholesterol; HDL= high density lipoproteins; TG= triglycerides; HbA1c= hemoglobin A1C; TyG= triglyceride-glucose index.
[3] Bold indicates statistically significant results (p>0.01*, 0.01≥p>0.001**, p≤0.001***)

Other CMR factors were not significantly different across trace minerals tertiles (table 1).

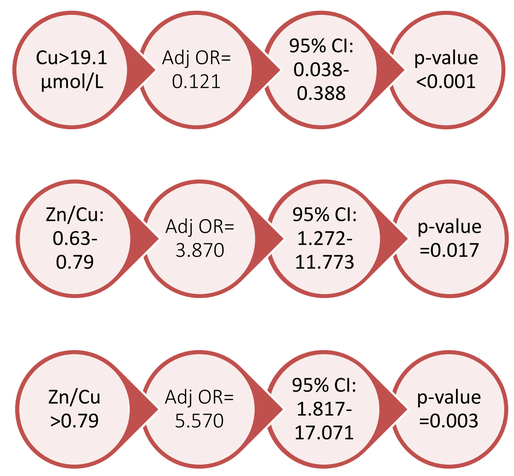
Figure 2: Partial Correlation between cardiometabolic indicators and trace minerals



Zn was not strongly correlated with CMR factors (p-value>0.01) (figure 2). Moreover, Zn was not significantly associated with any CMR factors while Cu was negatively associated with high DBP and HDL. Zn/Cu ratio was only significantly negatively associated with high SBP in the second tertile but was positively associated with low HDL in the third tertile.

RESULTS CONT.

Figure 3: Association between serum Cu and Zn/Cu and MetS



Zn was not associated with MetS (figure 3). Furthermore, the highest Cu tertile was significantly associated with low rate of MetS. However, MetS rate increased by more than 5.5 folds with the increase in Zn/Cu ratio in T3.

There were no differences observed in Zn, Cu levels and Zn/Cu ratio between participants with and without MetS (results not shown).

CONCLUSION

In conclusion, we did not report any association between serum Zn and CMR factors or MetS. Furthermore, high serum Cu, >15.8 µmol/L, had a protective effect on DBP, HDL and MetS. Serum Zn/Cu ratio was found to protect against high SBP only in the medium serum levels (0.63-0.79 µmol/L), however serum Zn/Cu ratio >0.79 µmol/L increased the risk of having low HDL. Also, Zn/Cu ratio >0.63 µmol/L increased the risk of MetS.

LIMITATIONS

First and most important, the study design, which is cross sectional, fails to conclude a causation between the minerals and cardiometabolic markers. Second, the sample size might be too small to represent the population being studied.

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