

# Pediatric Metabolic Syndrome & Minerals



## Antenatal micronutrient supplementation reduces metabolic syndrome in 6- to 8-year-old children in rural Nepal

- Previously, we showed that antenatal micronutrient supplementation increases birth weight in a malnourished rural South Asian setting, but the long-term effects are unknown. Between 1999 and 2001, pregnant women were sector-randomized to receive from early pregnancy through 3 mo postpartum daily micronutrient supplements containing either vitamin A alone as the control or with folic acid; folic acid+iron; folic acid+iron+zinc; or a multiple micronutrient supplement that included the above nutrients plus 11 others. From 2006 to 2008, 3524 children (93% of surviving children) were revisited between the ages of 6 and 8 y. Blood pressure, BMI, waist circumference, glycated hemoglobin, cholesterol, triglycerides, glucose, insulin, and the urinary microalbumin:creatinine ratio were assessed among children. Insulin resistance was estimated using the homeostasis model assessment (HOMA) and metabolic syndrome was defined using a modified National Cholesterol Education Program definition. None of the micronutrient supplement combinations affected blood pressure, cholesterol, triglycerides, glucose, insulin, or HOMA. There was a reduced risk of microalbuminuria ( $\geq 3.40$  mg/mmol creatinine) in the folic acid [odds ratio (OR), 0.56; 95%CI, 0.33-0.93;  $P = 0.02$ ] and folic acid+iron+zinc (OR, 0.53; CI, 0.32-0.89;  $P = 0.02$ ) groups and a reduced risk of metabolic syndrome in the folic acid group (OR, 0.63; CI, 0.41-0.97;  $P = 0.03$ ). Maternal supplementation with folic acid or folic acid+iron+zinc reduced the risk of kidney dysfunction and, to some extent, metabolic syndrome among children at 6-8 y of age. Supplementation with multiple micronutrients had no such effect. Future follow-up studies are needed to examine long-term supplementation effects on risk of chronic diseases in adults.
- [Stewart CP](#), [Christian P](#), [Schulze KJ](#), [Leclercq SC](#), [West KP Jr](#), [Khatry SK](#). Antenatal micronutrient supplementation reduces metabolic syndrome in 6- to 8-year-old children in rural Nepal. [J Nutr](#). 2009 ;139(8):1575-81.

# Effect of zinc supplementation on insulin resistance and components of the metabolic syndrome in prepubertal obese children

• **OBJECTIVE:** Zinc, an essential trace element and a component of many enzymes, is involved in the synthesis, storage and release of insulin. The aim of the present study was to assess the effect of zinc supplementation on insulin resistance and components of the metabolic syndrome in prepubertal obese children.

**DESIGN:** This triple-masked, randomized, placebo-controlled cross-over trial was conducted among 60 obese Iranian children in 2008. Pertinent clinical findings, fasting serum glucose, insulin and lipid profile were assessed. Participants were randomly assigned to two groups of equal number; one group received 20mg elemental zinc and the other group received placebo on a regular daily basis for eight weeks. After a 4-week wash-out period, the groups were crossed over.

**RESULTS:** The mean age of participants was 9.1 +/- 1.1 years. After receiving zinc, the mean fasting plasma glucose (FPG), insulin and HOMA-IR decreased significantly, while body mass index (BMI), waist circumference (WC), LDL-C and triglycerides (TG) did not significantly change. After receiving placebo, the mean FPG, insulin and HOMA-IR increased significantly, while BMI, WC, LDL-C and TG showed a non-significant increase.

**CONCLUSION:** Besides lifestyle modification, zinc supplementation might be considered as a useful and safe additional intervention treatment for improvement of cardiometabolic risk factors related to childhood obesity.

• [Hashemipour M, Kelishadi R, Shapouri J, Sarrafzadegan N, Amini M, Tavakoli N, Movahedian-Attar A, Mirmoghtadaee P, Poursafa P. Effect of zinc supplementation on insulin resistance and components of the metabolic syndrome in prepubertal obese children. Hormones \(Athens\). 2009 ;8\(4\):279-85.](#)

# Dietary zinc intake is inversely associated to metabolic syndrome in male but not in female urban adolescents

• **OBJECTIVE:** To evaluate the relationship of copper and zinc dietary intakes with metabolic syndrome (MetS) in adolescents.

**METHODS:** The sample consisted of 1,311 adolescents aged 11-16 years, and MetS definition by de Ferranti et al. was used. Nutritional intakes, anthropometrical and biochemical markers were measured.

**RESULTS:** In males, highest quartile of zinc intake was inversely associated with MetS without and with adjustment by covariables. Without adjustment, highest quartile of copper intake was inversely associated (marginal significance) with MetS, but with adjustment, the relationship was not maintained. Likewise in male gender, elevated waist circumference was the only MetS component inversely associated with highest quartiles of zinc (without and with adjustment) and copper (significant in crude analysis and marginal significant in adjustment by covariables) intakes. In the girls, only waist circumference was significant and inversely associated with highest quartiles of zinc and copper intakes but the association did not remain significant after adjustments.

**DISCUSSION:** In the adolescents of this study, zinc intake could be more associated to a clustering of anthropometric, vascular, and metabolic alterations than to these alterations separately, and also it is inversely related to this clustering (MetS). However, studies in other populations are necessary to confirm and explain the finding of exclusive association zinc intake-MetS in male gender adolescents. Further research is required to explore biomarkers of physiological processes (antioxidant function, blood flow regulation, and epigenetic modulation dependent of zinc) in relation to zinc intake and MetS in pediatric and adult populations.

• [Suarez-Ortegón MF, Ordoñez-Betancourth JE, Aguilar-de Plata C. Dietary zinc intake is inversely associated to metabolic syndrome in male but not in female urban adolescents. Am J Hum Biol. 2013 ;25\(4\):550-4.](#)

## Iron in child obesity. Relationships with inflammation and metabolic risk factors

- Iron (Fe) sequestration is described in overweight and in its associated metabolic complications, i.e., metabolic syndrome (MetS) and non-alcoholic liver fatty disease (NAFLD); however, the interactions between Fe, obesity and inflammation make it difficult to recognize the specific role of each of them in the risk of obesity-induced metabolic diseases. Even the usual surrogate marker of Fe stores, ferritin, is influenced by inflammation; therefore, in obese subjects inflammation parameters must be measured together with those of Fe metabolism. This cross-sectional study in obese youth (502 patients; 57% girls):  $11.4 \pm 3.0$  years old ( $x \pm SD$ ); BMI z score  $5.5 \pm 2.3$ ), multivariate regression analysis showed associations between Fe storage assessed by serum ferritin with risk factors for MetS and NAFLD, assessed by transaminase levels, which were independent of overweight and the acute phase protein fibrinogen. Further studies incorporating the measurement of complementary parameters of Fe metabolism could improve the comprehension of mechanisms involved.
- [Bouglé D, Brouard J. Iron in child obesity. Relationships with inflammation and metabolic risk factors. \*Nutrients\*. 2013 ;5\(6\):2222-30.](#)

## Relationship between Serum Levels of Body Iron Parameters and Insulin Resistance and Metabolic Syndrome in Korean Children

- **OBJECTIVES:** An increase in serum ferritin and levels of the cleaved soluble form of transferrin receptor (sTfR) are related to several metabolic conditions. We evaluated the relationship between body iron status indicators, including ferritin and sTfR, and insulin resistance and metabolic syndrome (MetS) in Korean children.
- **METHODS:** A cross-sectional study was conducted on 1350 children in Korea. Anthropometrical parameters; lipid profiles; levels of glucose, insulin, and leptin; and iron status indicators, including sTfR, serum ferritin, serum iron, total iron-binding capacity (TIBC), and transferrin saturation (TS), were analyzed.
- **RESULTS:** Although serum sTfR levels were significantly higher in boys than in girls (2.20 vs. 2.06 mg/L,  $p < 0.0001$ ), serum iron and TS were higher in girls than in boys (101.38 vs. 95.77 mg/L,  $p = 0.027$  and 30.15 vs. 28.91%,  $p = 0.04$ , respectively). Waist circumference (WC) and leptin were most significantly associated with body iron indicators when adjusted for age and sex. After adjusting for age, sex, and WC, sTfR levels showed the strongest positive association with leptin levels ( $p = 0.0001$ ). Children in the highest tertile for homeostasis model assessment-insulin resistance (HOMA-IR) had higher TIBC ( $p = 0.0005$ ) and lower serum iron ( $p = 0.0341$ ), and the lowest TS ( $p < 0.0001$ ) after adjustment for confounders. Children with higher sTfR were most significantly associated with risk of MetS compared with those lower sTfR ( $p = 0.0077$ ).
- **CONCLUSION:**
  - The associations of serum levels of iron metabolism markers with leptin levels, HOMA-IR, and MetS suggest that iron-related factors may involve insulin resistance and MetS.
- [Lee HJ, Jang HB, Park JE, Park KH, Kang JH, Park SI, Song J.](#) Relationship between Serum Levels of Body Iron Parameters and Insulin Resistance and Metabolic Syndrome in Korean Children. [Osong Public Health Res Perspect.](#) 2014;5(4):204-10.

# Association of serum concentrations of magnesium and some trace elements with cardiometabolic risk factors and liver enzymes in adolescents: the CASPIAN-III Study

• This study aims to investigate the association of serum concentrations of magnesium (Mg), selenium (Se), chromium (Cr), and copper (Cu) with cardiometabolic risk factors and liver functions in Iranian children and adolescents. This case-control study was conducted under a national surveillance program. It comprised 320 students, aged 10-18 years, in two groups of equal number with or without metabolic syndrome (MetS). Serum concentrations of Mg and abovementioned trace elements were measured by atomic absorption spectrophotometry. Median regression analysis and different models of logistic regression were used to determine the associations of these elements with cardiometabolic risk factors. In the MetS group, the median of Mg, Se, Cr, and Cu was lower or equal to controls. Mg had significant inverse association with some MetS components; however, the corresponding figure was stronger for the simultaneous association of Mg, Se, Cr, and Cu with MetS components. The binary logistic regression revealed that Mg was a significant protective factor against MetS ( $P = 0.0001$ ). Likewise, by considering the simultaneous association of Mg, Se, Cr, and Cu with MetS, Se was a significant protective factor against MetS. The corresponding figures were not significant for Cr and Cu. Se and Cu had significant inverse association with liver enzymes. The protective role of Mg and Se against MetS and liver enzymes, as well as the associations of these elements with some cardiometabolic risk factors and liver enzymes in the pediatric age group should be considered in future preventive and interventional studies.

• [Kelishadi R, Ataei E, Motlagh ME, Yazdi M, Tajaddini MH, Heshmat R, Ardalan G. Association of serum concentrations of magnesium and some trace elements with cardiometabolic risk factors and liver enzymes in adolescents: the CASPIAN-III Study. \*Biol Trace Elem Res.\* 2015 ;163\(1-2\):97-102.](#)

## Association of blood cadmium level with cardiometabolic risk factors and liver enzymes in a nationally representative sample of adolescents: the CASPIAN-III study

• **INTRODUCTION:** This study aimed to determine the association of blood cadmium level with cardiometabolic risk factors and liver enzymes in adolescents.

**METHODS:** This case control study comprised 320 Iranian adolescents, 160 with metabolic syndrome and an equal number of controls. They were selected from participants of a nationwide survey entitled the CASPIAN-III study. Cadmium was measured by atomic absorption method.

**RESULTS:** The mean age of the case and control groups was not significantly different ( $15.3 \pm 2.6$  versus  $14.63 \pm 2.5$  years, resp.,  $P > 0.05$ ). The mean cadmium level was near double-fold higher than the standards of the World Health Organization, without significant difference between the MetS and control groups ( $10.09 \pm 2.21$ ,  $9.97 \pm 2.38$   $\mu\text{g/L}$ , resp.,  $P > 0.05$ ). Cadmium level had positive but nonsignificant correlations with diastolic blood pressure, serum triglycerides, fasting blood glucose, LDL-C, and liver enzymes.

**CONCLUSION:** Cadmium level had positive but nonsignificant association with some cardiometabolic risk factors and liver enzymes. The associations did not reach statistical significant level, and this may be because of the high levels of cadmium in both groups studied or because of the young age group of participants. Controlling environmental pollutants shall be a priority for the prevention of chronic diseases.

• Kelishadi R, [Askarieh A](#), [Motlagh ME](#), [Tajadini M](#), [Heshmat R](#), [Ardalan G](#), [Fallahi S](#), [Poursafa P](#). [Association of blood cadmium level with cardiometabolic risk factors and liver enzymes in a nationally representative sample of adolescents: the CASPIAN-III study. J Environ Public Health. 2013;2013:142856.](#)



## Association of serum lead and mercury level with cardiometabolic risk factors and liver enzymes in a nationally representative sample of adolescents: the CASPIAN-III study

- This study aims to determine the difference of serum Pb and Hg levels in adolescents with or without metabolic syndrome (MetS) and the association of serum levels of these heavy metals with cardiometabolic risk factors and liver enzymes in Iranian adolescents. The study population consisted of 320 adolescents (160 with MetS and 160 healthy controls). The relationship between serum heavy metals and cardiometabolic risk factors was assessed by linear regression. The odds ratios (OR) of having metabolic syndrome across Pb and Hg quartiles were determined by multiple logistic regression analysis. The mean (SD) of Pb and Hg concentrations were higher in adolescents with MetS than in those without it (0.83 (0.27) and 0.17 (0.01) vs. 0.65 (0.15) and 0.10 (0.08)  $\mu\text{g/L}$ ,  $P = 0.01$  and  $0.0001$ , respectively). Increase in serum Pb and Hg was associated with increase in some cardiometabolic risk factors. Among boys and girls, diastolic blood pressure (DBP), fasting blood glucose, total cholesterol (TC), triglycerides (TG), and alanine aminotransaminase increased significantly across quartiles of serum Pb. Among girls, SBP, DBP, TC, and TG had a significant increase across Hg quartiles. The corresponding figure among boys was significant for SBP, DBP, and TG. Higher quartiles of Pb increased the risk of having MetS (OR 95 % CI 3.10, 2.25-4.27), the corresponding figure was 2.03, 1.75-3.16, across Hg quartiles. Our study showed significant associations between serum Pb and Hg levels with cardiometabolic risk factors in adolescents. In future surveys, the role of potential confounders should be considered more extensively. The clinical significance of these findings needs to be confirmed in longitudinal studies. By considering the origins of chronic diseases from early life, controlling environmental pollutants should be considered as a health priority for primordial or primary prevention of noncommunicable diseases.
- [Poursafa P, Ataee E, Motlagh ME, Ardalan G, Tajadini MH, Yazdi M, Kelishadi R. Association of serum lead and mercury level with cardiometabolic risk factors and liver enzymes in a nationally representative sample of adolescents: the CASPIAN-III study. Environ Sci Pollut Res Int. 2014 ;21\(23\):13496-502.](#)

## Assessment of dietary calcium intake on metabolic syndrome frequency in obese children and adolescents

• **INTRODUCTION:** High dietary calcium intake has an impact on reduction of adipose tissue, as in prevention and treatment of obesity and metabolic syndrome (MS). The aim of the study was to evaluate the influence of dietary calcium on appearance MS in children and adolescents.

**MATERIALS AND METHODS:** The study included 150 patients in the age range of 7-18 years with obesity. In each child, the bioelectrical impedance analysis, waist circumference, blood pressure, lipids (enzymatic method), Oral Glucose Tolerance Test (OGTT) with marking of glucose, insulin blood levels (RIA method), and estimation of nutritional status had been made. The standard deviation score of body mass index (SDS BMI), waist to hip ratio (WHR), insulin resistance (HOMA-IR) was calculated. MS was recognized according Cook criteria.

**RESULTS:** All patients had waist circumference greater than the 90 percentile. Boys had more often an abnormal lipids profile than girls. Both, high blood pressure and HOMA-IR  $>3$  were found in over half of studied patients. The diet of many patients had too much fat and saccharose intaking. Only 20% of children consumed normal value of calcium. The observed intaking more than 20 mg of calcium per ideal body mass (i.b.m) per 24 hours had higher % FAT, SDS BMI, waist circumference, HOMA-IR, and insulin. MS was recognized more often in this group.

**CONCLUSIONS:** Insufficient dietary calcium intake could have an effect on some parameters of metabolic syndrome.

- [Czerwonogrodzka A, Pyrzak B, Majcher A, Rumińska M, Rymkiewicz-Kluczyńska B, Jeznach-Steinhagen A.](#) Assessment of dietary calcium intake on metabolic syndrome frequency in obese children and adolescents. [Pediatr Endocrinol Diabetes Metab.](#) 2008;14(4):231-5.

## Mediterranean-style diet reduces metabolic syndrome components in obese children and adolescents with obesity

• **BACKGROUND:** The beneficial effects of the Mediterranean diet have been amply proven in adults with cardiovascular risk factors. The effects of this diet have not been extensively assessed in pediatric populations with obesity, insulin resistance (IR) and metabolic syndrome (MetS). The aim of this study was to assess the efficacy of the Mediterranean style diet (MSD) to decrease cardiovascular risk factors in children and adolescents with obesity.

**METHODS:** Participants were randomly assigned to a MSD rich in polyunsaturated fatty acids, fiber, flavonoids and antioxidants (60% of energy from carbohydrate, 25% from fat, and 15% from protein, (n = 24); or a standard diet (55% of carbohydrate, 30% from fat and 15% from protein, (n = 25), the caloric ingest was individualized. At baseline and 16-week of intervention, the glucose, triglycerides (TG), total cholesterol (TC), HDL-C, LDL-C were measured as well as the body composition and anthropometric data. The diet compliance was determined by the 24-hour recalls. Paired Student's t and Macnemar's test were used to compare effects in biochemical, body composition, anthropometric, and dietary variables.

**RESULTS:** The MSD group had a significantly decrease in BMI, lean mass, fat mass, glucose, TC, TG, HDL-C and LDL-C. ( $p < 0.05$ ); the diet compliance increased consumption of omega 9 fatty acids, zinc, vitamin E, selenium, and decreased consumption of saturated fatty acids ( $p < 0.05$ ). The standard diet group decrease in glucose levels and frequency of glucose  $>100$  mg/dL ( $p < 0.05$ ).

### **CONCLUSION:**

The MSD improves the BMI, glucose and lipid profile in children and adolescents with obesity and any MetS component.

• [Velázquez-López L](#), [Santiago-Díaz G](#), [Nava-Hernández J](#), [Muñoz-Torres AV](#), [Medina-Bravo P](#), [Torres-Tamayo M](#).

Mediterranean-style diet reduces metabolic syndrome components in obese children and adolescents with obesity. [BMC Pediatr](#). 2014 ;14:175.

Thank  
you

