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Original article

Lower serum zinc levels are associated with unhealthy metabolic status in normal-weight adults: The 2010 Korea National Health and Nutrition Examination Survey

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Abstract

Aim. – This study investigated whether serum zinc concentration is associated with glucose tolerance, insulin resistance and metabolic health status in Korean adults.

Methods. – Subjects with available serum zinc levels were recruited from the fifth Korea National Health and Nutrition Examination Survey (KNHANES V) cohort. Those in the highest quartile on homoeostasis model assessment for insulin resistance (HOMA-IR) and with a body mass index (BMI) of 18.5–25 kg/m^2 were classified as metabolically obese and normal weight (MONW).

Results. – A total of 1813 subjects with a mean age of 45.2 ± 0.5 years and a mean BMI of 24.01 ± 0.11 kg/m^2 were enrolled. Those in the lower serum zinc quartiles exhibited higher levels of fasting blood glucose and insulin resistance indices compared with those in the higher quartiles. However, these associations were positive only in normal-weight subjects. Those categorized as MONW exhibited significantly lower serum zinc levels than the metabolically healthy and normal weight (MHNW) subjects (131.6 ± 3.0 μg/dL *vs* 141.7 ± 2.8 μg/dL, respectively; $P = 0.0026$), whereas serum zinc levels did not differ according to metabolic health in obese subjects. The odds ratio for being categorized as MONW was 4.12 (95% CI: 1.75, 9.72) among those in the lowest serum zinc quartile compared with those in the highest quartile even after adjusting for possible confounding factors.

Conclusion. – Lower serum zinc levels were associated with unhealthy metabolic status in normal-weight adults. Further prospective studies are required to define the role of zinc in metabolic health.

Keywords: Diabetes mellitus; Insulin resistance; Korea; Metabolic health; Obesity; Zinc

Abbreviations: BMI, Body Mass Index; BP, blood pressure; CI, confidence interval; DM, diabetes mellitus; HDL, high-density lipoprotein; HOMA-β, homoeostasis model assessment estimate of β-cell function; HOMA-IR, homoeostasis model assessment of insulin resistance; IFG, impaired fasting glucose; KNHANES, Korea National Health and Nutrition Examination Survey; LDL, low-density lipoprotein; MHNW, metabolically healthy and normal weight; MHO, metabolically healthy obesity; MONW, metabolically obese but normal weight; MOO, metabolically obese obesity; NGT, normal glucose tolerance; OR, odds ratio; QUICKI, quantitative insulin sensitivity check index; SE, standard error; WC, waist circumference.

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1. Introduction

Zinc is an essential trace element involved in the synthesis, storage and release of insulin [1]. Zinc is also a structural component of key antioxidant enzymes such as superoxide dismutase and glutathione peroxidase [2]. This suggests that abnormal zinc levels might induce alterations of insulin metabolism and oxidative stress that could ultimately lead to increased susceptibility to diabetes mellitus (DM) and metabolic syndrome.

Several studies have reported that lower serum zinc levels and higher urinary zinc excretion occur in patients with DM compared with non-diabetic subjects [3,4]. A large population-based prospective study revealed that higher zinc intakes might be associated with a lower risk of type 2 DM in women [5]. However, others have reported that serum zinc concentrations do not differ according to glucose tolerance [6,7].

The relationship between zinc and the metabolic syndrome is also controversial. Several studies have reported that higher zinc intakes have protective effects against metabolic syndrome [8,9], whereas positive relationships [10,11] or no relationships [12,13] have been observed in other study populations.

The discrepancies surrounding serum zinc levels and metabolic status might be a consequence of the different characteristics of the examined study populations. People with metabolically obese and normal weight (MONW) phenotypes are characterized by impaired insulin sensitivity and increased levels of adiposity, despite having a normal body mass index (BMI). Another subset of individuals exhibiting lower degrees of insulin resistance and favourable metabolic profiles despite their high BMIs are classified as having metabolically healthy obesity (MHO) [14,15]. However, in spite of being categorized into the same group according to BMI criteria, the different metabolic health status of these individuals could lead to clinical outcomes that differ from those of their counterparts [16]. Yet, until now, no studies have evaluated the relationship between serum zinc level and metabolic health. Therefore, our present study aimed to investigate whether serum zinc concentration is associated with metabolic health, as determined by the degree of insulin resistance and using large-scale survey data from a Korean population.

2. Methods

2.1. Study population

The present study was based on data acquired in the first year (2010) of the fifth Korea National Health and Nutrition Examination Survey (KNHANES V), a cross-sectional and nationally representative survey conducted by the Division of Chronic Disease Surveillance of the Korea Centers for Disease Control and Prevention. The sampling frame design was based on the 2005 population and housing census in Korea, and used a rolling sampling protocol that involved complex, stratified, multistage, clustered and probability samples. The overall survey consisted of a health interview survey, a nutrition survey and a health examination survey. Data were collected through household interviews and physical measurements, with blood sampling performed at specially equipped examination centres. Additional details regarding this survey have been described elsewhere [17–19].

From a total of 8958 subjects, serum zinc levels were measured in randomly selected subjects from each of the study's regional, gender and age groups ($n = 1988$). Equal numbers (12 or 13) of subjects were selected from each study subregion and from the different gender and age groups. No more than two individuals were selected from the same family. Excluded were 175 subjects, who were underweight (BMI < 18.5 kg/m^2, $n = 91$), pregnant ($n = 8$), or had any type of malignancy ($n = 16$) or liver/kidney disease ($n = 15$), or who were missing values for baseline characteristics ($n = 45$). Ultimately, the study population consisted of 1813 subjects aged 19 or older (906 men and 907 women). Written informed consent was obtained from all participants, and the Institutional Review Board of The Catholic University of Korea approved the study protocol (No. KC14OISI0714).

2.2. Health and nutrition survey

Medical history information and lifestyle habits were collected through self-reported questionnaires. Current smokers were defined as those either currently smoking or those who had ever smoked at least five packs of cigarettes during their lifetime. Subjects who drank more than 30 g/day of alcohol were designated heavy drinkers. Regular exercise was defined as strenuous physical activity performed for at least 20 min three times a week. Total caloric intake was assessed through a 24-h dietary recall questionnaire administered by a trained dietitian. Results were calculated using the food composition table developed by the Korean National Rural Resources Development Institute.

2.3. Measurements

Anthropometric measurements were taken with subjects wearing light clothing, and BMI was calculated as the subject's weight (kg) divided by the square of the subject's height (m^2). Waist circumference (WC) was measured in standing position at a level midway between the lower rib margin and the iliac crest. Blood pressure (BP) was measured three times on the right arm, using a mercury sphygmomanometer (Baumanometer; W.A. Baum Co. Inc., Copiague, NY, USA), with the subject in a seated position after at least 5 min of resting. Blood samples were drawn after at least 8 h of fasting, and were immediately processed, refrigerated and transported to the central testing institute (NeoDin Medical Institute, Seoul, Korea). Serum insulin was analyzed by immunoradiometric assay using INS-IRMA kits (BioSource Europe S.A., Nivelles, Belgium). Serum zinc concentration was measured by inductively coupled plasma mass spectrometry (ICP-MS) assay (PerkinElmer, Waltham, MA, USA). Serum levels of glucose, total cholesterol, triglyceride and high-density lipoprotein (HDL) cholesterol were measured enzymatically with an automatic chemistry analyzer (Hitachi 7600; Hitachi, Ltd, Tokyo, Japan), and low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula [20]. Assay