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Liver enzymes and vitamin D levels in metabolically healthy but obese individuals: Korean National Health and Nutrition Examination Survey

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ABSTRACT

Objective. Increased liver enzymes and decreased vitamin D levels are associated with insulin resistance and type 2 diabetes. We examined liver enzymes and vitamin D levels in metabolically healthy but obese (MHO) individuals and compared the values with those of other body size phenotypes in the Korean population.

Materials/Methods. A total of 16,190 people over the age of 18 years were analyzed using data from the Fourth Korean National Health and Nutrition Examination Survey, which is a nationally representative survey. Body size phenotypes were classified into four groups by body mass index (BMI) and number of metabolic syndrome components.

Results. The prevalence of MHO was 14.9% in the entire population and 47.7% in the obese population. In a correlation analysis adjusted for age, sex, and BMI, AST and ALT levels were positively correlated with insulin resistance and cardiometabolic risk factors of the metabolic syndrome, whereas vitamin D level was negatively correlated with these variables. MHO individuals had significantly lower concentrations of AST and ALT compared to metabolically abnormal obese (MAO) subjects, although vitamin D levels were not significantly different. Furthermore, a multiple logistic regression analysis revealed that MHO individuals had lower risk of liver enzyme abnormality compared to MAO after adjusting for potential confounding factors. However, the risk of vitamin D deficiency was not significantly different among groups with different body size phenotypes.

Conclusions. Although both liver enzymes and vitamin D levels are related to insulin resistance and metabolic syndrome, only liver enzymes were independently associated with MHO phenotype.

Abbreviations: MHO, Metabolically healthy but obese; CVD, Cardiovascular disease; NAFLD, Nonalcoholic fatty liver disease; NHANES III, Third National Health and Nutrition Examination Survey in the United States; KNHANES IV, Fourth Korean National Health and Nutrition Examination Survey; BMI, Body mass index; 25(OH)D, 25-hydroxyvitamin D; OR, Odds ratio; CI, Confidence interval; MAO, Metabolically abnormal obese.

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1. Introduction

Metabolically healthy but obese (MHO) individuals comprise a subset of the obese population, and they have drawn attention due to their unique metabolic features. These individuals, despite having excessive body fat, display a favorable metabolic profile, including high insulin sensitivity, normal lipid and blood pressure, and low circulating inflammatory markers [1–3]. Calori et al. reported that MHO individuals did not show increased all-cause, cancer, or cardiovascular disease (CVD) mortality compared with non-obese insulin-sensitive subjects in a 15-year follow-up study [4].

Obesity is closely associated with nonalcoholic fatty liver disease (NAFLD), which is a hepatic manifestation of metabolic syndrome [5]. Stefan et al. found that ectopic fat in skeletal muscle and particularly the liver was lower in the obese–insulin-sensitive group than in the obese–insulin-resistant group [6]. In a recent study of 103 postmenopausal Caucasian women, Messier et al. reported that MHO individuals, defined by insulin sensitivity index, had significantly lower concentrations of liver enzymes than insulin-resistant at-risk subjects [7]. However, the relationship between liver enzymes and MHO phenotype has not been established in other age groups or ethnicities.

Vitamin D has numerous functions beyond calcium and bone metabolism. The cross-sectional survey of the Third National Health and Nutrition Examination Survey in the United States (NHANES III) showed an inverse relationship between vitamin D level and diabetes, possibly involving insulin resistance, in non-Hispanic whites and Mexican Americans [8]. Moreover, there was an inverse relationship between serum concentration of vitamin D and the prevalence of metabolic syndrome [9]. Recently, Barchetta et al. reported that low 25-hydroxyvitamin D (25(OH)D) level is associated with the presence of NAFLD, independent of metabolic syndrome, diabetes and insulin-resistant profiles [10]. However, to the best of our knowledge, no previous studies have explored vitamin D level in MHO individuals.

The present study examined concentrations of liver enzymes and vitamin D in MHO individuals and compared them with those of other body size phenotypes using representative data from the Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV).

2. Research design and methods

2.1. Subjects and data collection

This study analyzed data from the KNHANES IV, a cross-sectional and nationally representative survey conducted by the Division of Chronic Disease Surveillance of the Korean Center for Disease Control and Prevention. The KNHANES consists of four different surveys designed to evaluate the general health and nutrition status of Koreans: a health interview survey, a health behavior survey, a health examination survey, and a nutrition survey. Details of the KNHANES have been published in previous studies [11,12]. Over the three year KNHANES IV survey (from 2007 to 2009), 23,631 individuals participated in health interviews and health examination surveys (4246 in 2007, 9307 in 2008, and 10,078 in 2009). Among them, 17,664 people older than 18 years were selected for this study. Subjects with missing data concerning fasting glucose, metabolic syndrome components, or body mass index (BMI) were excluded (n = 1474), resulting in a total of 16,190 subjects for this analysis.

2.2. Subject classifications

Asian populations have a higher risk of type 2 diabetes and cardiovascular disease compared to other populations with the same BMI. Therefore, the WHO defines obesity in adult Asians as a BMI ≥25 kg/m^2, compared to individuals of other ethnicities who are considered obese with a BMI ≥30 kg/m^2 [13]. In this study, the components of metabolic syndrome were defined as follows: (i) systolic/diastolic blood pressure ≥130/85 mmHg or antihypertensive medication use, (ii) fasting triglycerides ≥1.7 mmol/l, (iii) high-density lipoprotein <1.3 mmol/l or lipid-lowering medication use, and (iv) fasting glucose ≥5.6 mmol/l. Waist circumference was not considered when classifying body size phenotype due to its covariability with BMI. Body size phenotypes were divided into four groups based on BMI value, diabetes status, and the number of metabolic syndrome components (normal weight with 0/1 vs. ≥2 components/diabetes and obesity with 0/1 vs. ≥2 components/diabetes) according to the criteria of Wildman et al. [2]. The obese group with 0/1 components was regarded as MHO, and the obese group with ≥2 components/diabetes was classified as the metabolically abnormal obese (MAO) group.

2.3. Definition of abnormal ALT and vitamin D levels

In a recent study including 665 biopsy-proven Korean subjects, the upper limit of normal ALT value was reported as 33 IU/L for men and 25 IU/L for women [14]. The present study used the same criteria to define abnormal liver function. Vitamin D deficiency in the present study was defined as a serum circulating 25(OH)D level below 20 ng/ml (50 nmol/L), according to the most recent Endocrine Society clinical practice guidelines [15].

2.4. Measurement of anthropometric and laboratory parameters

Waist circumference was measured from the narrowest point between the lower borders of the rib cage and the iliac crest. Blood pressure was measured when the subject was seated after a 10-min rest period. Two systolic and diastolic blood pressure readings were recorded with a 5-min interval and were averaged for analysis. Fasting blood samples were collected in the morning after at a fast of at least 8 h. Blood samples were centrifuged, refrigerated at the examination site, and transferred in iceboxes to a central laboratory in Seoul the same day they were collected. Plasma glucose, total cholesterol, triglyceride, HDL cholesterol, AST, and ALT levels were measured using an autoanalyzer (ADVIA 1650, Siemens, Germany) from 1st Jan, 2007 to 15th Feb, 2008 and with a Hitachi 7600 (Hitachi, Japan) from 20th Feb, 2008 to 31st Dec, 2009. Serum 25(OH)D level was measured using a Gamma