Clinica Chimica Acta 458 (2016) 12–17

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

Relationship between non-alcoholic fatty liver disease, metabolic syndrome and insulin resistance in Korean adults: A cross-sectional study

Ji Young Kim [a,b], Choae Lee [a,b], Minsuk Oh [a,b], Jee-Aee Im [c], Ji-Won Lee [d], Sang Hui Chu [e,f], Hyangkyu Lee [e,f,*], Justin Y. Jeon [a,b,**]

[a] Department of Sport and Leisure Studies, Yonsei University, Seoul, Republic of Korea
[b] Exercise Medicine Center for Cancer and Diabetes Patients, ICONS, Yonsei University, Seoul, Republic of Korea
[c] Sport and Medicine Research Center, INTOTO Inc., Seoul, Republic of Korea
[d] Department of Family Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea
[e] Department of Clinical Nursing Science, Yonsei University College of Nursing, Seoul, Republic of Korea
[f] Nursing Policy and Research Institute, Biobehavioral Research Center, Yonsei University, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 9 October 2015
Received in revised form 22 March 2016
Accepted 22 March 2016
Available online 25 March 2016

Keywords:
Non-alcoholic fatty liver disease
Metabolic syndrome
Insulin resistance

ABSTRACT

Background: We investigated the independent and combined impact of obesity and nonalcoholic fatty liver disease (NAFLD) on components and prevalence of metabolic syndrome in Korean adults.
Methods: This study included 1695 adults (500 males and 1,195 females), who took part in a regular health check-up at the community-based health promotion center. Participants were divided according to degree of adiposity and the presence of NAFLD. The components and prevalence of metabolic syndrome were compared.
Results: Fasting glucose was significantly higher in nonobese participants with NAFLD compared to obese participants without NAFLD. Logistic regression analysis revealed that the presence of NAFLD was associated with 3.63 times increased prevalence of metabolic syndrome (95% CI: 1.21–10.86) while obesity without NAFLD was associated with 3.84 times increased prevalence of metabolic syndrome (95% CI: 1.57–9.36) in male. In female, the presence of NAFLD was associated with 5.56 times higher prevalence of metabolic syndrome (95% CI: 2.53–12.23) while obesity without NAFLD had 3.46 times increased prevalence of metabolic syndrome (95% CI: 1.64–7.33).
Conclusions: NAFLD is associated with the prevalence of metabolic syndrome, independent of adiposity. In females, NAFLD may be a more important factor than obesity for risk of metabolic syndrome.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a clinicopathological syndrome that is characterized by accumulation of fat in the liver without significant alcohol abuse [1]. In recent years, the prevalence of NAFLD has dramatically increased [2], and is the most common cause of chronic liver disease in the world [3,4].

It has previously been reported that obesity is a significant predictor of metabolic syndrome [5,6]. Components of metabolic syndrome are closely linked to obesity and a great deal of attention has been paid to the relationship between obesity and metabolic syndrome [7–9]. However, recent studies suggest that NAFLD is an additional feature of metabolic syndrome [10,11]. Uchil et al. [12] reported that the prevalence of metabolic syndrome was significantly higher in people with NAFLD than people without NAFLD (47% vs. 23%). Esteghamati et al. [13] also showed that elevated alanine aminotransferase (ALT), another indirect indicator of fatty liver, was significantly correlated with fasting insulin and homeostasis model assessment of insulin resistance (HOMA-IR). The role of insulin resistance in the pathogenesis of NAFLD is supported by pathophysiologic considerations, laboratory investigations, and clinical associations [14]. Although it is clear that both obesity and NAFLD contributed to the development of metabolic syndrome, the independent and combined association of obesity and NALFD on the prevalence of metabolic syndrome has not been fully elucidated.

2. Materials and methods

2.1. Study population

This study recruited 1695 participants (500 males and 1,195 females), who participated in a regular check-up program between

* Correspondence to: H. Lee, Department of Clinical Nursing Science, Yonsei University College of Nursing, 50 Yonsei-ro, Seodaemun-Gu, Seoul, Republic of Korea.
** Correspondence to: J.Y. Jeon, Department of Sport and Leisure Studies, Yonsei University, Seoul, Republic of Korea.
E-mail addresses: hkyulee@yuhs.ac (H. Lee), jjeon@yonsei.ac.kr (J.Y. Jeon).

http://dx.doi.org/10.1016/j.cca.2016.03.018
0009-8981/

2004 and 2007 at a community-based health promotion center in Seoul, Korea. Participants with a history of liver cirrhosis including malignancy, chronic viral hepatitis, auto-immune hepatitis, hereditary hemochromatosis, Wilson's disease and drug-induced liver disease were excluded. In addition, participants with ALT activities > 40 IU/l and/or GGT activities > 100 IU/l were excluded to rule out participants who may have liver diseases other than NAFLD [15]. All participants signed a consent form prior to participation in the study.

2.2. Anthropometric measurements

Body weight and height were measured to the nearest 0.1 kg and 0.1 cm using an electronic scale and a stadiometer. BMI was defined as weight/height^2 (kg/m^2). Waist circumference (WC) was measured at a point midway between the tenth rib and the iliac crest and recorded to the centimeter [16]. Blood pressure was measured twice by a skilled nurse following at least ten minutes of rest, and the mean value was recorded for study purposes.

2.3. Biochemical measurements

Blood samples were collected after a minimum of 12 h of overnight fasting. Serum triglycerides (TG), fasting glucose, high density lipoprotein cholesterol (HDL-C), total cholesterol (TC) and high sensitive C-reactive protein (hs-CRP) concentrations were evaluated by an ADVIA 1650 Chemistry analyzer (Siemens). If serum TG concentrations were <400 mg/dl, low density lipoprotein cholesterol (LDL-C) was calculated using Friedewald's formula [17]. Fasting insulin concentrations were measured using an Immulite 2000 in immunoradiometric assay (Siemens). Insulin resistance was calculated by HOMA-IR [18], where HOMA-IR = [fasting insulin (μIU/ml) * fasting glucose (mmol/l)/22.5].

2.4. Sonographic evaluation

Experienced technicians used abdominal ultrasonography with a 5 MHz transducer and a high-resolution B-mode scanner (ALOKA SSD-650CL) to diagnose fatty liver disease according to the following four criteria including vascular blurring, deep-echo attenuation, hepatorenal echo contrast and the brightness of liver [19]. The overall gain, initial gain, and time gain compensation settings were kept within a narrow range and all ultrasonography images were stored as photocopies. Gastroenterologists reviewed the photocopies and made the diagnosis of fatty liver. Fatty infiltration was classified qualitatively based on the severity of fatty liver disease according to subjective assessment of the contrast between the hepatic parenchyma and the renal cortex, in terms of echo intensity [20].

2.5. Definitions

This study used class III obesity classification based on the World Health Organization (WHO) criteria for Asians [21], where a BMI ≥ 25 is considered obese, and a BMI < 25 is nonobese. Metabolic syndrome was defined according to the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) [22] and the Korean Society for the Study of Obesity criteria [23]. Participants who met three or more of the following criteria were diagnosed with metabolic syndrome: blood pressure ≥ 130/85 mm Hg or use of antihypertensive medication by a patient with a history of hypertension; fasting glucose ≥ 100 mg/dl or use of medication to treat elevated glucose, triglycerides ≥ 150 mg/dl or use of medication to treat high triglycerides; HDL-cholesterol ≤ 40 mg/dl in males and ≤50 mg/dl in females, or use of medication to treat low HDL-cholesterol concentrations; WC ≥ 90 cm in males and ≥85 cm in females.

2.6. Statistical analysis

Data were analyzed using SPSS 21.0 software. Values were expressed as the mean ± SD for normally distributed variables or as numbers (percentage). An independent *t*-test was used to compare baseline characteristics between participants with and without NAFLD. Comparisons between participants with and without NAFLD and according to BMI levels were performed using analysis of variance (ANOVA), followed by a post hoc Scheffe for males and analysis of covariance (ANCOVA) with post hoc Bonferroni for females. To determine the combined impact of adiposity and NAFLD, we classified participants into 4 groups according to their BMI (≥25 vs. < 25) and NAFLD diagnosis (Yes/No) as follows; nonobese without NAFLD; nonobese with NAFLD; obese without NAFLD; and obese with NAFLD. *P*-values less than 0.05 were considered significant. Odds ratios (ORs) and 95% confidence intervals (CIs) for risk factors of metabolic syndrome were calculated using a standard logistic regression model adjusted for age in males, and age and menopausal status in females.

3. Results

3.1. General characteristics of participants

A total of 1695 participants (500 males and 1,195 females), including 347 participants (20.5%) with NAFLD (143 males, 28.6%; 204 females, 17.8%), were included in the final analysis. Anthropometric and biochemical characteristics of participants at baseline are described in Table 1. Weight, BMI, WC, fasting glucose, TC, TG, ALT, GGT, fasting insulin and HOMA-IR were significantly higher and HDL-cholesterol concentrations were lower in males with NAFLD compared to those without NAFLD at baseline ($P < 0.05$). Age, weight, BMI, WC, SBP, DBP, fasting glucose, TC, TG, LDL-C, ALT, GGT, fasting insulin, and HOMA-IR were significantly higher, while HDL-C was lower, in females with NAFLD compared to those without NAFLD.

3.2. Relationship between NAFLD, components of metabolic syndrome and insulin resistance in males

Nonobese participants with NAFLD had significantly higher BMI, fasting glucose, TG, ALT and lower HDL-C compared to those without NAFLD (Table 2). In addition, fasting glucose was statistically higher in the nonobese group with NAFLD compared to the nonobese and obese participants without NAFLD. The obese participants with NAFLD had statistically higher TG, fasting insulin and HOMA-IR compared to the obese group without NAFLD, despite a similar BMI between the two groups. Since there was a statistical difference in BMI among groups, additional analyses were performed after controlling for BMI. However, only minor differences were observed, even after controlling for BMI.

3.3. Relationship between NAFLD, components of metabolic syndrome and insulin resistance in females

Since participants with NAFLD had higher BMI and age, all analyses were performed after controlling for these two parameters (Table 3). The nonobese participants with NAFLD had statistically higher fasting glucose, TG, ALT, GGT, fasting insulin and HOMA-IR, as well as lower HDL-C compared with both the nonobese and obese groups without NAFLD. Among obese participants, those with NAFLD had significantly higher fasting glucose, ALT, GGT and hs-CRP compared to those without NAFLD. Interestingly, obese participants without NAFLD had significantly lower fasting glucose, TG, ALT, and GGT and higher HDL-C compared to nonobese participants with NAFLD.