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ORIGINAL CONTRIBUTION

Oxidative balance score and serum γ-glutamyltransferase level among Korean adults: a nationwide population-based study

A.-Ra Cho[1] · Yu-Jin Kwon[2] · Hyoung-Ji Lim[3] · Hye Sun Lee[4] · Sinae Kim[4] · Jae-Yong Shim[5] · Hye-Ree Lee[1] · Yong-Jae Lee[1]

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Abstract
Purpose The oxidative balance score (OBS) comprises dietary and non-dietary lifestyle pro-oxidants and antioxidants. Elevated serum γ-glutamyltransferase (GGT) level has currently emerged as a biomarker of oxidative stress. In this study, we examined whether OBS was inversely associated with serum GGT level and whether OBS could be a useful marker to predict GGT among Korean adults.
Methods This cross-sectional study was based on data obtained from the 2010 and 2011 Korea National Health and Nutrition Examination Survey. 2087 men and 2071 women were included in final analysis. The OBS was divided into five equal interval categories, and GGT was dichotomized into low and high using its sex-specific median value. Multiple logistic regression analysis was conducted to assess the association between OBS categories and high GGT.
Results Compared with the lowest OBS category as reference, the multivariable adjusted ORs (95% CIs) for the highest OBS category of men and women were 0.05 (0.01–0.19) and 0.27 (0.09–0.78), respectively (p for trend <0.01).
Conclusion A higher OBS that indicates a predominance of antioxidant over pro-oxidant exposure was strongly inversely associated with GGT level among Korean adults.

Keywords Oxidative balance score · Oxidative stress · γ-Glutamyltransferase · Inflammation · Biomarker

Introduction

γ-Glutamyltransferase (GGT), a microsomal membrane-binding protein, presents both in serum and on the external surface of most human cells, particularly in detoxifying organs such as the liver and kidneys [1]. GGT plays an important role in maintaining the homeostasis of glutathione (L-γ-glutamyl-L-cysteinyl-glycine), which is a very potent antioxidant against free radicals [reactive oxygen and nitrogen species (RONS)] [1, 2]. Serum GGT has long been regarded a marker of hepatobiliary diseases or alcohol consumption. More recently, elevated GGT level has become an independent predictor for cardiometabolic diseases, which are increasingly viewed as inflammatory diseases. Thus, elevated GGT level may be an epiphenomenon of abundant extracellular glutathione degradation [3].

Oxidative stress is thought to result from a predominance of pro-oxidant to antioxidant exogenous and endogenous exposures/conditions, which can increase reactive oxygen and nitrogen species (RONS; also referred to as

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✉ Yong-Jae Lee
ukyjhome@yuhs.ac

[1] Department of Family Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 135-720, Republic of Korea

[2] Department of Family Medicine, Yong-in Severance Hospital, Yonsei University College of Medicine, Yong-in City, Republic of Korea

[3] Department of Family Medicine, Chungbuk National University Hospital College, Cheongju, Republic of Korea

[4] Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul, Republic of Korea

[5] Department of Family Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

free radicals), which can damage macromolecules, and disrupt redox signaling, which can cause aberrant cell signaling [4, 5]. RONS can either be produced endogenously, as the result of an intracellular mechanism in mitochondria and cytosolic enzyme systems, or exogenously, from external agents, such as diet, medications, and environmental toxins. Increased oxidative stress from so-called pro-oxidants has been proposed to activate specific redox-sensitive signaling pathways and damage proteins, lipids and DNA. Consequently, the accumulative effects of oxidative stress are thought to contribute to the etiology of wide spectrum of diseases, including cardiovascular disease, metabolic syndrome and some types of cancers [6–8].

The effects of individual exogenous pro-oxidants and antioxidants are supported by a considerable body of evidence from basic science and animal studies. High intakes of certain nutrients, such as vitamin C [9] and β-carotene [10], protect against oxidative stress, while pro-oxidant factors, including smoking [11], alcohol drinking [12], and iron intake [13], increase RONS production. Although, the individual effects of pro-oxidants and antioxidants are important, due to a web-like interaction involving multiple factors [14], a combined measure of various dietary and non-dietary lifestyle pro-oxidants and antioxidants could be a more accurate indicator of overall oxidative stress. In 2007, Goodman et al. [15] introduced an oxidative balance score (OBS) to reflect an overall pro-oxidant and anti-oxidant exposure balance. A higher OBS indicates a predominance of antioxidant over pro-oxidant exposures. Several studies recently assessed the association between this summary score and the risk of colorectal cancer, hypertension, and all-cause mortality [16–22].

Based on the available literatures, we hypothesized that a higher OBS is associated with a lower serum GGT level. Thus, we examined whether OBS was inversely associated with serum GGT level and whether OBS could be a useful marker to predict GGT among Korean adults.

Methods

Study population

This study was based on data obtained from the Fifth Korea National Health and Nutrition Examination Survey (KNHANES-V), a nationally representative survey conducted by the Korea Centers for Disease Control and Prevention between 2010 and 2012. Only 2010 and 2011 data were used in this study, as the level of GGT was not available in the 2012 KNHANES. The target population of this survey was non-institutionalized Korean citizens. The sampling units were households selected through a stratified, multistage, probability-sampling design that was based on geographic area, sex, and age-group using household registries. To produce results representative of the entire Korean population, sampling weights indicating the probability of being sampled were assigned to each participant. Participants answered a four-part questionnaire that included a health interview, evaluation of health behavior, a health examination, and a nutrition survey. For the 2010–2011 KNHANES, citizens were informed that they had been randomly selected as a household to voluntarily participate in the nationally representative survey conducted by the Korean Ministry of Health and Welfare, and that they had the right to refuse to participate in accordance with the National Health Enhancement Act supported by the National Statistics Law of Korea. All study participants provided written informed consent. The Korea Centers for Disease Control and Prevention also obtained participant consent to use blood samples for additional academic purposes. The health examination included a medical history, a physical examination, a questionnaire about health-related behaviors, and anthropometric and biochemical measurements. The physical examination was performed by trained medical staff following standardized procedures.

In this study, 17,476 participants were included in the 2010 and 2011 KNHANES. Of these, we excluded 7071 participants aged <19 years or >65 years, because children, adolescents, and the elderly have small changes in GGT levels with age [2]. Additionally, subjects meeting any of the following criteria were excluded: a history of liver cancer, hepatitis B or C, a pregnant state, or use of oral contraceptives. Participants who took dietary supplements were also excluded due to the incomplete information of calculated nutrients from the supplements. After these exclusions, 2087 men and 2071 women were included in final analysis. The KNHANES was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention (IRB No. 2010-02CON-21-C, 2011-02CON-06-C).

Data collection

The 24-h dietary recall method was used to collect data of food consumed by participants during the previous 24 h. Intake of total fat, iron, β-carotene, and vitamin C were computed using the 7th revision Standard Food Composition Table produced by the Korea National Rural Resources Development Institute [23]. Participants were also asked about their lifestyle behaviors, including cigarette smoking and alcohol consumption. Smoking history was categorized based on self-reported smoking status and the number of cigarettes current smokers smoked per day. Alcohol consumption was assigned to four categories based on how frequently participants consumed any type of alcohol. The short form of the International Physical Activity Questionnaire (IPAQ) was used to assess physical activity.

Additionally, all subjects were instructed to record their daily engagement in mild, moderate, or vigorous intensity of activity during the previous 7 day period. Then, we estimated the quantity of physical activity (MET-h/wk) on the basis of physical activity frequency and intensity [24]. Body mass index (BMI) was calculated as the ratio of weight (kg) to height^2 (m^2). Blood pressure was measured in the right arm using a standard mercury sphygmomanometer (Baumanometer, Copiague, NY, USA). Two systolic and diastolic blood pressure readings were recorded at 5-min intervals and averaged for analysis. After 12-h overnight fasting, the blood samples were obtained from an antecubital vein. Fasting plasma glucose (FPG), total cholesterol, triglycerides, high density lipoprotein (HDL) cholesterol and GGT level were measured using a Hitachi 700-110 chemistry analyzer (Hitachi, Japan).

Definition of OBS

The OBS consisted of eight components that were selected based on a priori information about their relationship to oxidative stress. In this study, the OBS included dietary pro-oxidants (total fat intake and iron intake), dietary antioxidants (β-carotene intake and vitamin C intake) as well as non-dietary lifestyle pro-oxidants (cigarette smoking, alcohol consumption and obesity) and non-dietary lifestyle antioxidants (physical activity). Several important nutrients such as vitamin E, and use of medications such as aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) were not included, because these data were unavailable in the 2010 and 2011 KNHANES.

Continuous variables, such as total daily fat intake, iron intake, β-carotene intake, vitamin C intake, BMI and physical activity, were divided into four categories based on sex-specific quartile values. For antioxidants, the first to fourth quartiles were assigned 0 to 3 points, respectively, whereas the point assignment for pro-oxidants was the reverse, 0 points for the highest quartile and 3 points for the lowest quartile. A similar scoring approach was used for categorical variables. Smoking history was categorized into non-smokers, former smokers, current smokers <1 pack/day, and current smokers ≥1 pack/day, each assigned 3 through 0 points, respectively. For alcohol consumption, never or <1 drinks/mon, 1–4 drinks/mon, 2–3 drinks/week, and ≥4 drinks/week received 3, 2, 1, and 0 points, respectively. The overall OBS was calculated by summing the points assigned for each component; higher OBS scores reflected a predominance of antioxidant exposure. The OBS component assignment scheme is shown in Table 1.

Statistical analysis

Because GGT values differ significantly by sex, all analyses were performed separately for each sex. The OBS was divided into five equal interval categories, with the lowest category used as the reference group. The baseline characteristics of the study participants were reported across OBS categories. Differences in characteristics across OBS categories were summarized using either analysis of variance for continuous variables or the Chi-square test for categorical variables. Pearson and Spearman correlation coefficients were calculated for correlations of GGT level with each OBS component, age, total energy intake, fasting plasma glucose, total cholesterol, triglyceride, HDL cholesterol, blood pressure, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) among men and women. The odds ratios (ORs) and 95% confidence intervals (CIs) for high GGT according to OBS categories were

Table 1 The scheme of oxidative balance score (OBS) assignment

OBS components	Score assignment
Dietary pro-oxidants	
Total fat	0 = fourth quartile, 1 = third quartile, 2 = second quartile, 3 = first quartile
Iron	0 = fourth quartile, 1 = third quartile, 2 = second quartile, 3 = first quartile
Dietary antioxidants	
β-Carotene	0 = first quartile, 1 = second quartile, 2 = third quartile, 3 = fourth quartile
Vitamin C	0 = first quartile, 1 = second quartile, 2 = third quartile, 3 = fourth quartile
Non-dietary lifestyle pro-oxidants	
Smoking history	0 = current smoker (≥1 pack/day), 1 = current smoker (<1 pack/day), 2 = former smoker, 3 = nonsmoker
Alcohol	0 = ≥4 drinks/wk, 1 = 2–3 drinks/wk, 2 = 1–4 drinks/mon, 3 = never or <1 drink/mon
BMI	0 = fourth quartile, 1 = third quartile, 2 = second quartile, 3 = first quartile
Non-dietary lifestyle antioxidants	
Physical activity	0 = first quartile, 1 = second quartile, 2 = third quartile, 3 = fourth quartile

BMI body mass index

estimated using logistic regression analyses after adjusting for other confounding variables. GGT as a dependent variable was dichotomized into low and high using its sex-specific median value as the cutoff, 32 IU/L for men and 15 IU/L for women, respectively. The multivariable adjusted ORs (95% CIs) for high GGT according to the dietary and lifestyle OBS (treated as continuous variables) were also obtained to assess the relative contributions of the dietary and lifestyle OBS to high GGT. Additional sensitivity analyses were conducted to examine the impact of individual OBS components by removing each component from the total score and controlling for it as a covariate. All analyses were performed using SPSS for Windows (version 20.0; SPSS Inc., Chicago, Ill., USA). All statistical tests were two-sided and statistical significance was determined at a p value <0.05.

Results

After calculation using the assignment scheme shown in Table 1, the OBS ranged from 3 to 21 points in men, and 5 to 22 points in women. The baseline characteristics of men and women by OBS equal interval category are summarized in Tables 2 and 3, respectively. There were no significant differences at baseline in age among either men or women. As expected, dietary antioxidants and physical activity were higher, and dietary pro-oxidants and BMI were lower in higher OBS categories. Compared with those in the lowest OBS category, participants in the highest OBS category were less likely to be heavy smokers and drinkers. Serum GGT level was lower in higher OBS categories among both men and women.

Pearson and Spearman correlations between various factors including the eight OBS components and GGT are listed in Table 4. Of the eight components of OBS, the strongest correlations with GGT were observed for smoking history ($r=0.21$) and alcohol drinking ($r=0.37$) among men, and BMI ($r=0.17$) among women.

Table 5 shows the results of multiple logistic regression analyses to assess the association between OBS equal interval categories and GGT. Compared with the lowest OBS category as reference, the multivariable adjusted ORs (95% CIs) for the highest OBS category of men and women were 0.05 (0.01–0.19) and 0.27 (0.09–0.78), respectively (p for trend <0.01). In addition, the results of logistic regression analyses to assess the associations of dietary and lifestyle OBS with GGT are presented in Table 6. Using OBS as

Table 2 Baseline characteristics of men ($n=2087$) by OBS equal interval category

Characteristics	Category 1 ($n=55$)	Category 2 ($n=563$)	Category 3 ($n=798$)	Category 4 ($n=613$)	Category 5 ($n=58$)
OBS range	3–6	7–10	11–13	14–17	18–21
Age (years)	41.0 ± 1.7	40.4 ± 0.5	39.9 ± 0.5	39.4 ± 0.6	39.3 ± 2.3
Daily fat intake (g/day)	73.1 ± 6.3	67.3 ± 2.1	54.8 ± 1.5	48.5 ± 2.1	27.4 ± 2.8*
Daily iron intake (mg/day)	21.3 ± 2.0	19.7 ± 0.6	17.5 ± 0.4	16.1 ± 0.4	12.7 ± 0.8*
Daily β-carotene intake (μg/day)	2824.7 ± 341.9	4020.8 ± 233.9	5133.1 ± 348.7	5601.2 ± 247.2	9165.8 ± 1809.7*
Daily vitamin C intake (mg/d)	59.3 ± 4.8	91.2 ± 4.0	113.7 ± 3.4	142.7 ± 4.8	170.3 ± 10.5*
Current smoker ≥1 pack/day	34 (62.7)	249 (47.0)	147 (19.3)	54 (9.2)	0 (0.0)*
Alcohol drinking ≥4 drinks/week	26 (46.9)	139 (23.2)	115 (12.3)	29 (3.5)	1 (1.7)*
BMI (kg/m^2)	27.0 ± 0.5	25.3 ± 0.1	24.2 ± 0.1	23.0 ± 0.1	22.0 ± 0.4*
Physical activity (MET-h/week)	12.0 ± 2.5	31.3 ± 2.4	46.3 ± 2.6	70.2 ± 4.0	84.1 ± 9.2*
Total energy intake (kcal/day)	2836.7 ± 134.5	2777.6 ± 58.2	2524.4 ± 44.6	2405.3 ± 47.5	1979.0 ± 129.4*
Fasting plasma glucose (mg/dL)	101.8 ± 2.2	101.1 ± 1.4	97.1 ± 0.9	95.9 ± 1.0	92.5 ± 1.8*
Total cholesterol (mg/dL)	192.3 ± 5.0	192.9 ± 1.6	187.6 ± 1.5	182.5 ± 1.5	174.5 ± 4.8*
Triglyceride (mg/dL)	208.9 ± 20.0	202.9 ± 8.4	155.4 ± 6.0	124.7 ± 3.7	110.0 ± 14.7*
HDL cholesterol (mg/dL)	49.0 ± 1.3	48.5 ± 0.6	49.9 ± 0.4	50.9 ± 0.6	54.8 ± 2.0*
Systolic blood pressure (mmHg)	124.2 ± 2.3	121.7 ± 0.7	119.2 ± 0.5	118.6 ± 0.6	117.9 ± 2.1*
Diastolic blood pressure (mmHg)	82.7 ± 1.7	82.1 ± 0.5	79.6 ± 0.4	78.9 ± 0.5	76.4 ± 1.9*
AST (IU/L)	31.6 ± 2.3	26.5 ± 0.6	23.4 ± 0.4	23.2 ± 0.6	22.2 ± 0.9*
ALT (IU/L)	36.3 ± 5.9	31.5 ± 1.1	25.6 ± 0.6	24.4 ± 1.0	19.4 ± 1.0*
GGT (IU/L)	73.2 ± 5.9	64.3 ± 3.3	45.0 ± 2.0	37.1 ± 1.8	31.8 ± 5.6*

Data are expressed as the mean ± SD or number (%)

SD standard deviation, *BMI* body mass index, *MET* metabolic equivalents, *HDL* high density lipoprotein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *GGT* γ-glutamyltransferase

*p values <0.05 based on the analysis of variance for continuous variables and Chi-square test for categorical variables

Table 3 Baseline characteristics of women ($n=2071$) by OBS equal interval category[a]

Characteristics	Category 1 ($n=39$)	Category 2 ($n=490$)	Category 3 ($n=904$)	Category 4 ($n=553$)	Category 5 ($n=85$)
OBS range	5–8	9–12	13–15	16–18	19–22
Age (years)	38.4 ± 2.3	35.6 ± 0.6	38.1 ± 0.5	38.4 ± 0.6	40.0 ± 1.5
Daily fat intake (g/day)	51.4 ± 3.7	50.0 ± 1.8	38.2 ± 1.0	30.9 ± 1.4	20.2 ± 0.9*
Daily iron intake (mg/day)	16.8 ± 1.3	13.2 ± 0.4	12.9 ± 0.3	13.2 ± 0.5	10.4 ± 0.6*
Daily β-carotene intake (μg/day)	1872.0 ± 401.4	2556.3 ± 139.1	3735.2 ± 190.1	5076.4 ± 312.1	5833.8 ± 640.6*
Daily vitamin C intake (mg/day)	48.1 ± 6.1	71.3 ± 3.5	95.6 ± 2.6	142.1 ± 6.6	159.1 ± 10.3*
Current smoker ≥1 pack/day	4 (5.6)	5 (1.6)	3 (0.5)	0 (0.0)	0 (0.0)*
Alcohol drinking ≥4 drinks/week	3 (4.0)	22 (5.0)	11 (1.5)	1 (0.1)	0 (0.0)*
BMI (kg/m^2)	26.7 ± 0.7	24.2 ± 0.2	22.8 ± 0.1	21.9 ± 0.1	21.3 ± 0.3*
Physical activity (MET-h/week)	16.4 ± 8.0	18.7 ± 2.4	28.8 ± 1.8	48.1 ± 3.0	64.3 ± 8.0*
Total energy intake (kcal/d)	2127.6 ± 98.2	1896.2 ± 44.3	1729.9 ± 26.7	1645.9 ± 35.5	1393.0 ± 46.3*
Fasting plasma glucose (mg/dL)	96.2 ± 2.5	92.8 ± 0.9	90.9 ± 0.4	90.0 ± 0.7	91.7 ± 1.7*
Total cholesterol (mg/dL)	194.8 ± 5.4	181.3 ± 1.7	183.8 ± 1.3	180.6 ± 1.6	184.6 ± 4.3
Triglyceride (mg/dL)	149.4 ± 20.3	104.9 ± 4.3	96.7 ± 2.3	94.8 ± 3.8	92.3 ± 7.5
HDL cholesterol (mg/dL)	57.5 ± 2.5	56.4 ± 0.7	57.2 ± 0.5	57.2 ± 0.7	57.4 ± 1.6
Systolic blood pressure (mmHg)	117.7 ± 1.7	111.7 ± 0.8	111.7 ± 0.6	110.8 ± 0.8	109.2 ± 1.5*
Diastolic blood pressure (mmHg)	77.4 ± 1.3	72.6 ± 0.4	72.7 ± 0.3	73.0 ± 0.5	70.8 ± 1.1*
AST (IU/L)	18.2 ± 0.6	19.0 ± 0.4	18.3 ± 0.2	18.6 ± 0.3	18.4 ± 0.7
ALT (IU/L)	17.3 ± 1.1	17.3 ± 0.6	15.8 ± 0.4	15.5 ± 0.5	15.3 ± 1.3
GGT (IU/L)	29.5 ± 4.9	22.4 ± 1.2	18.6 ± 0.5	17.6 ± 0.7	17.1 ± 1.1*

Data are expressed as the mean ± SD or number (%)

SD standard deviation, *BMI* body mass index, *MET* metabolic equivalents, *HDL* high-density lipoprotein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *GGT* γ-glutamyltransferase

*p values <0.05 based on the analysis of variance for continuous variables and Chi-square test for categorical variables

a continuous variable, the multivariable adjusted ORs (95% CIs) for lifestyle OBS of men and women were 0.70 (0.66–0.75) and 0.83 (0.77–0.89), respectively, while the association between dietary OBS and GGT was not statistically significant.

Supplementary Table 1 presents the sensitivity analyses in which the observed results for the original 8-component OBS (examined as a continuous variable) were compared with the corresponding results after each OBS component was removed from the score one at a time and included in the model as a covariate. Removing any single OBS component did not produce meaningful changes in the ORs estimates among either men or women.

Discussion

We examined the association between the OBS and serum GGT level in a representative sample of Korean adults. In this cross-sectional study, we found that participants in the highest OBS category relative to those in the lowest had approximately 20-fold (men) and 3.7-fold (women) lower odds for having elevated GGT levels in a dose–response manner. Our findings are in agreement with the results of previous studies that found serum GGT level was positively associated with oxidative stress or inflammation markers [16, 25]. In a previous study, the authors found a statistically significantly positive association between GGT and leukocyte counts and C-reactive protein (CRP) levels among 4562 Korean adults [26]. Cellular GGT metabolizes glutathione and allows for precursor amino acids to be reutilized for intracellular glutathione synthesis. This mechanism can lead to continuous recycling of glutathione, the most important non-protein antioxidant in cells. Although the relationship between cellular and serum GGT remains unclear, a number of current studies suggest that serum GGT within its normal range might be an early and sensitive enzyme for oxidative stress [27–30].

Several studies also reported associations between the OBS and biomarkers of oxidative stress, including plasma F_2-isoprostanes, fluorescent oxidation products, and CRP. Lakkur et al. [25] found a higher OBS to be statistically significantly associated with a lower level of F2-isoprostanes, but a higher level of fluorescent oxidation products. Kong et al. [16] found a negative association between the OBS and circulating F_2-isoprostanes and CRP levels in a case-control study of colorectal adenoma. Although F_2-isoprostanes has been reported as a useful

Table 4 Correlation between various factors including OBS components and GGT

	Men		Women	
	r^a	p value[b]	r^a	p value[b]
Age (years)	0.15	<0.01	0.16	<0.01
Daily fat intake (g/day)	−0.08	<0.01	−0.05	0.01
Daily iron intake (mg/day)	−0.01	0.74	0.02	0.26
Daily β-carotene intake (μg/day)	−0.02	0.31	0.03	0.19
Daily vitamin C intake (mg/day)	−0.04	0.06	−0.02	0.24
Smoking history	0.21	<0.01	0.08	<0.01
Alcohol drinking	0.37	<0.01	0.12	<0.01
BMI (kg/m^2)	0.11	<0.01	0.17	<0.01
Physical activity (MET-h/week)	0.03	0.12	0.01	0.68
Total energy intake (kcal/day)	0.01	0.70	−0.03	0.10
Fasting plasma glucose (mg/dL)	0.18	<0.01	0.16	<0.01
Total cholesterol (mg/dL)	0.18	<0.01	0.18	<0.01
Triglyceride (mg/dL)	0.41	<0.01	0.28	<0.01
HDL cholesterol (mg/dL)	0.02	0.19	0.01	0.76
Systolic blood pressure (mmHg)	0.19	<0.01	0.15	<0.01
Diastolic blood pressure (mmHg)	0.18	<0.01	0.14	<0.01
AST (IU/L)	0.56	<0.01	0.43	<0.01
ALT (IU/L)	0.41	<0.01	0.59	<0.01

BMI body mass index, *HDL* high density lipoprotein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase

[a]Correlation coefficients (r)

[b]p Values were calculated using Pearson's correlation analysis for continuous variables and Spearman's correlation analysis for cigarette smoking and alcohol drinking

measure of oxidative stress in previous studies [31], it is not routinely evaluated in standard clinical practice. Moreover, as previously documented, elevated GGT level has emerged as a simple, global, cost-effective biomarker of oxidative stress through a series of epidemiological and experimental studies [32, 33]. In this regard, we used serum GGT as a biomarker of oxidative stress in the present study, and found an inverse association between the OBS and serum GGT level. We believe that the present study is the first study to evaluate the association between the OBS and a plasma biomarker of oxidative stress in a Korean population.

Our study has several limitations. First, single 24-h dietary recall method which may not capture day-to-day variability was used to assess dietary pro-oxidants and antioxidants. Although 24-h dietary recalls are less prone to recall bias and their validity has been demonstrated by previous studies [34, 35], several 24-h dietary recalls over extended period of time are needed to assess more accurate associations between dietary components and GGT. Second, all the OBS components were equally weighted in the overall score. An equal weighting approach may not accurately reflect the real relative biologic contributions of individual pro-oxidant and antioxidant exposures. In a previous cohort study, conducted to investigate associations between the OBS and all-cause, cancer, and non-cancer mortality in the United States, Kong et al. [22] used four different weighting schemes, including equal weights and literature-based weights. However, very similar results were observed across all weighting methods. Third, the OBS was limited to dietary and non-dietary lifestyle exposures. Endogenous factors that affect DNA damage and repair, cell growth, and cell death, such as cellular antioxidant enzymes, were not included [36, 37]. Fourth, we did not consider the threshold effect of antioxidants which may exert toxic pro-oxidant activities at higher doses or under certain conditions [38]. In addition, we assumed all pro-oxidant and antioxidant properties were related linearly to oxidative stress, and assigned a higher or lower score to increasing quartiles of antioxidant or pro-oxidant factors. Finally, this was a cross-sectional study in design and it was not possible to establish a causal relationship between the OBS and

Table 5 Results of multiple logistic regression analyses to assess the associations between OBS categories and high GGT

OBS categories	Men		Women	
	Unadjusted OR (95% CI)	Multivariable OR[a] (95% CI)	Unadjusted OR (95% CI)	Multivariable OR[a] (95% CI)
1	1.00	1.00	1.00	1.00
2	0.38 (0.16–0.88)	0.37 (0.16–0.85)	0.32 (0.13–0.79)	0.45 (0.17–1.18)
3	0.15 (0.06–0.35)	0.18 (0.08–0.41)	0.24 (0.10–0.59)	0.36 (0.14–0.92)
4	0.09 (0.04–0.21)	0.11 (0.05–0.24)	0.17 (0.07–0.42)	0.23 (0.09–0.61)
5	0.04 (0.01–0.12)	0.05 (0.01–0.19)	0.18 (0.06–0.48)	0.27 (0.09–0.78)
p for trend	<0.01	<0.01	<0.01	<0.01

The cutoff points of high GGT were determined as 32 IU/L for men and 15 IU/L for women, respectively, which corresponded to the sex-specific median value

OR odds ratio, *CI* confidence intervals

[a]Adjusted for age, total energy intake, fasting plasma glucose, total cholesterol, systolic blood pressure and alanine aminotransferase

Table 6 Results of logistic regression analyses to assess the associations of dietary and lifestyle OBS with high GG

Model	Men OR (95% CI)[a]	Women OR (95% CI)[a]
OBS original model	0.81 (0.78–0.85)	0.89 (0.85–0.93)
Dietary OBS, controlled for lifestyle components	0.97 (0.90–1.05)	0.96 (0.90–1.03)
Lifestyle OBS, controlled for dietary components	0.70 (0.66–0.75)	0.83 (0.77–0.89)

OR odds ratio, *CI* confidence intervals

[a]Adjusted for age, total energy intake, fasting plasma glucose, total cholesterol, systolic blood pressure and alanine aminotransferase

serum GGT level. Further prospective studies including a larger number of participants over a longer period of time are warranted to confirm any potential cause-and-effect relationship.

In conclusion, a higher OBS, a composite measure that reflects a predominance of antioxidant over pro-oxidant exposure, was strongly inversely associated with GGT level among Korean adults. These findings may provide further support for the validity of the OBS and the use of GGT as a biomarker of oxidative stress.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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