Original Article

Serum and dietary antioxidant status is associated with lower prevalence of the metabolic syndrome in a study in Shanghai, China

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Objective: The aim of our study was to examine the association between the metabolic syndrome (MS) and serum antioxidant status. Methods: A cross-sectional study was conducted with 221 cases and 329 controls aged 18 to 65 years. Weight, height, body mass index, waist circumference, blood pressure, fasting blood glucose and lipids, as well as serum superoxide dismutase, glutathione peroxidase, malondialdehide, vitamins A, E, β-carotene and lycopene were examined. Intakes of antioxidants were also estimated. Results: Mean serum superoxide dismutase activity, β-carotene concentrations were significantly lower, malondialdehide was higher (p<0.05) in persons with the MS (after adjusting for age, sex) than those without. Superoxide dismutase, glutathione peroxidase, and β-carotene also decreased significantly (p<0.05) with increased number of components of the MS. Low levels of serum superoxide dismutase activity and β-carotene concentration appeared to be associated with the MS status. Moreover, dietary energy, carbohydrate, vitamin C, zinc and copper intake in the MS patients were lower, but fat intake were higher. Vitamins E, C and manganese intake decreased with the elevated number of the MS components. For zinc and manganese, a lower risk was observed for other quartile of intake compared with the first one. Inverse links between dietary fat, energy intake and serum antioxidant status were found in MS patients, meanwhile dietary vitamin C was positively related with serum antioxidant level. Conclusions: Serum antioxidant status was associated with a lower prevalence of the MS, and with lower dietary fat, energy intake and higher vitamin C intake.

Key Words: human, antioxidant, serum, diet, metabolic syndrome

INTRODUCTION

The metabolic syndrome (MS), a constellation of abdominal obesity, insulin resistance, dyslipidaemia, hyperglycemia, and hypertension, is a multiplex risk factor for both type 2 diabetes and cardiovascular disease.[1] The prevalence of MS, which varies according to different diagnostic criteria, is increasing to epidemic proportions not only in the urbanized world but also in developing nations. Over the last few decades, tremendous urbanization and economic development has led Chinese people into a new life pattern with over-nutrition and less physical activity, which was accompanied by higher prevalence of MS.[2] Although the exact mechanism leading to MS is still in the process of being elucidated, it is a complex interaction between genetic, metabolic, and environmental factors, and abdominal obesity and insulin resistance appear to play key roles in MS.[3]

It is well known that oxidative stress plays a considerable role in the pathogenesis of MS components and insulin resistance[4]. In the natural course, the production and activation of reactive oxygen species (ROS) is initially counterbalanced by a compensatory increase in antioxidant systems to maintain normal ROS level. However, the increase in antioxidant systems is eventually unable to offset the severe degree of ROS production, and may lead to modification of carbohydrates, lipids and proteins, and promotion of the development of MS and its associated complications.[4,5]

The natural antioxidant system of the human body consists of enzymatic (SOD, GSH-Px) and non-enzymatic (including, but not limited to, vitamins E, C, β-carotene, and lycopene) components. Cells may maintain their levels of antioxidants through dietary intake and/or *de novo* synthesis[4]. Several cross sectional and longitudinal epidemiologic studies have indicated inverse associations between MS and fruit, vegetables, or Mediterranean-style diets rich in fruit and vegetables, which have potent antioxidant properties and could account for these inverse associations.[6-10] Meanwhile, patients with MS were characterized with elevated oxidative stress and decreased antioxidant protection in comparison with those without MS, as evidenced by some studies.[4,8,11-14]

Although diet is the main external contributor to the regulation of serum antioxidant status, there are few stud

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ies, to the best of our knowledge, examining associations between serum antioxidant status and nutritional intake of MS patients in China. Therefore, the aim of the present study was to investigate these relationships in a case-control study in Shanghai, China. In this study, we measured serum antioxidant status by examining antioxidant enzymatic activity of Cu/Zn extracellular-SOD (Cu/Zn-Ec-SOD), GSH-Px, concentrations of β-carotenes, lycopene, vitamins A and E, and MDA in serum, and dietary antioxidant nutrients including vitamins A, E and C, zinc, selenium, copper, manganese were also examined.

MATERIALS AND METHODS

Subjects

Eligible participants aged 18 to 65 years were recruited in Shanghai by a multistage cluster random-sampling method, by which we selected randomly one district, then recruited participants from 2 communities according to residential distribution via simple random method. The MS diagnosis was based on the modified criteria of National Cholesterol Education Program ATP-III.[15] This criteria includes: abdominal obesity (waist circumference ≥90 cm for men and ≥80 cm for women), and 2 or more of the following: triglycerides >1.7, or treatment for dyslipidemia; high-density lipoprotein-cholesterol (HDL-C) <1.0 mmol/L in men and <1.3 mmol/L in women; blood pressure ≥130/85 mmHg or antihypertensive treatment; fasting blood glucose ≥5.5 mmol/L or treatment for diabetes. Persons were excluded if they took vitamin supplement during the previous 24 h. A total of 221 MS patients were diagnosed with MS through physical exam and lab measurements, and 329 controls were recruited due to the ratio of sex of MS patients. Our study has been approved by local review board of all participating institutions. Written informed consent was obtained from all participants before starting the study.

Anthropometric measurement

Participants were interviewed to obtain information including medical history on hypertension, diabetes, and dyslipidemia. Height and weight was measured while the subjects were barefoot and wearing only their underwear. BMI was calculated as weight in kilograms divided by the square of the height in meters. Waist circumference was measured by horizontally positioning a tape meter across the umbilicus, and hip circumference was measured at the maximum level of that. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured on the right upper arm of the subject in the sitting position, after at least 5 min of rest in a quiet environment, using a mercury sphygmomanometer.

Measurement of serum lipids and antioxidant status

Venous blood specimens were drawn after overnight fasting, centrifuged immediately for 15 minutes at 3000 rpm and 4°C for plasma separation, and stored at -40°C until assayed. Triglyceride (TG), total cholesterol (TC), and high-density lipoprotein-cholesterol (HDL-C) were measured enzymatically with specific commercially available kits (Nanjing jiancheng biotechnology Co.). Low-density lipoprotein-cholesterol (LDL-C) was calculated as described by Friedewald *et al.*[16] Fasting serum glucose was measured by the glucose-oxidase method. MDA, SOD and GSH-Px activity were analyzed by means of commercial kits (Nanjing jiancheng biotechnology Co). Insulin was measured with SN-695 Counter (Shanghai Hesuo Rihuan Photoelectric Instrument Co, Ltd) using radioimmune assay kit from Beijing Chemclin Biotech Co Ltd.

Vitamins A, E, β-carotene and lycopene in the serum were measured by a HP1100 LC-API4000 TQ Mass Spectrometer system (Applied Biosystems, USA). They were detected by their absorbance at 325, 292, 450, 472 nm respectively. Separation of these antioxidants was performed at 45°C on a hypersil ODS column (particle size = 4.6×250×5μm internal diameter; GL Science). For HPLC analysis, buffer A was made using 60% methanol, 20% acetonitrile, and 20% high-purity water. Buffer B was made by 53% acetonitrile, 26% methanol, and 21% tetrahydrofuran. A 20-μl serum was injected into the column equilibrated with buffer A. The elution gradient was as follows: 20% buffer B for 3.5 min; 98% buffer B for 4.5 min; and 98% buffer B for 12 min, 20% buffer B for 13 min. The flow rate was maintained at 1 ml/min.

Dietary assessment

Dietary intake was measured with a consecutive individual 3 day food diary, including two weekdays and one weekend. Research dieticians instructed the subjects with a booklet with letters representing small, medium, or large portions. The participants were asked to record a detailed description of all foods, beverages and supplements in 3 consecutive days. All records were checked by the dietitian at return and any incomplete information was clarified. The daily average of energy and nutrients intake was calculated by using the SY Nutrient Analysis System with Chinese food nutrients.

Statistical analyses

Continuous variables results were expressed as mean standard deviation of means for the parameters. Pearson's chi-square test was used to assess the relationship between the presence and absence of the MS and selected categorical variables. Student's t test was applied to compare differences in means between the two groups. One way ANOVA (analysis of variance) was conducted for comparing means in more than three groups. Serum antioxidant variables and dietary antioxidant intakes were distributed into quintiles for the regression analysis to better understand their relation with the MS. Logistic regression analysis was utilized to assess the association between serum antioxidant status, dietary antioxidant nutrients intake as dependent variables and the MS status. Statistical analyses were carried out with SPSS for Windows program16.0 package (SPSS, Chicago, IL, USA). Two-tailed *p*-values of 0.05 or less was considered statistically significant.

RESULTS

This study was performed in 221 subjects with the MS and 323 persons without the MS. The general characteristics of subjects with or without the MS are provided in Table 1. As would be expected, TG, BMI, insulin, waist circumference, hip circumference, and blood pressure

Table 1. General status of the subjects

Characteristics	Control Group	MS Group	*p* –value
Gender (Male/Female)	130/199	81/140	0.50
Age	53.3±5.83	54.2±5.73	0.07
TG (mmol/L)	1.18±0.82	2.13±1.28	<0.01
TC (mmol/L)	5.00±1.04	4.94±1.33	0.58
HDL-C (mmol/L)	1.35±0.31	1.28±0.47	0.04
LDL-C (mmol/L)	3.25±1.09	3.41±1.00	0.07
BMI	24.1±4.13	26.9±3.21	<0.01
Waistline (cm)	83.6±8.74	93.0±7.80	<0.01
Hipline (cm)	96.9±6.95	102±6.39	<0.01
Fasting plasma glucose (mmol/L)	4.87±1.28	5.67±2.00	<0.01
Insulin	8.02±3.40	11.1±5.71	<0.01
Systolic pressure (mmHg)	123±15.3	135±16.2	<0.01
Diastolic pressure (mmHg)	81.6±10.3	88.6±9.62	<0.01

Data are means ± *SD*. TG indicates Triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; BMI, body mass index.

Table 2. Oxidative stress parameters in the serum of subjects

	Control Group	MS Group	*p*-value †
SOD (U/mL)	50.4±15.4	47.7±16.2	0.022
GSH-Px (U/mL)	91.3±21.1	87.0±19.2	0.093
MDA (μmol/L)	5.87±2.69	6.74±3.66	0.010
Vitamin A (μmol/L)	0.62 ±0.25	0.62±0.21	0.906
Vitamin E (μmol/L)	12.1±4.13	12.9±5.00	0.300
Lycopene (mmol/L)	0.19±0.09	0.18±0.07	0.501
β-carotene (mmol/L)	0.38±0.24	0.28 ±0.19	0.015

Data are mean ± SD.
† Multivariable linear regression model adjusting for potential cofounders including: age (25–34, 35–44, 45–54, 55–64, 65–74 and 75+) and sex (male and female)

measurements were significantly higher in patients as compared to controls, and HDL was lower in patients (Table 1). There were no significant differences in TC and LDL levels between patients and controls. Sex distribution and age produced no differences between groups.

The mean of serum SOD, GSH-Px, MDA by MS status are provided in Table 2. After adjusting for potential confounding factors including age, sex, the activity of SOD, and the concentration of β-carotene was significantly lower for participants with MS compared to those without MS. Meanwhile, MDA was significantly higher in the case group than in controls. No significant differences in serum vitamin A, Vitamin E, lycopene were found between controls and the MS group. Table 3 indicate that serum SOD and GSH-Px decreased significantly, as the number of components of the MS increased, except for GSH-Px of subjects with 5 components of the MS; the participants with 3 or 4 components had lower GSH-Px activity in comparison with normal subjects.

Associations between serum antioxidant status and odds of the MS were shown in Table 4. The odds were 0.505 and 0.097 (p <0.05) in the highest quartile of the SOD and β-carotene compared with the lowest after adjusting age and sex.

Table 5 displays dietary intake of all subjects. Compared to those without the MS, the MS patients had significantly lower energy, carbohydrate, vitamin C, and zinc intake, but significantly higher fat intake, after adjusting for potential confounding factors including age, and sex. In addition, the dietary intake of vitamin E and

Table 3. Mean concentrations of serum oxidative stress parameters by the MS components among participants †

	Number of MS components in participants ‡					
	0 (*n*=74)	1 (*n*=142)	2 (*n*=59)	3 (*n*=140)	4 (*n*=66)	5 (*n*=19)
SOD (U/mL)	52.2±16.9	52.0±14.1	49.6±17.7	48.8±15.1	46.3±17.7*	43.0±10.1*
GSH-Px (U/mL)	95.8±24.3	89.9±20.5	90.6±20.9	85.6±18.8*	84.4±18.1*	94.8±23.4
MDA (μmol/L)	5.28±2.35	6.36±2.85	6.19±3.05	6.10±3.31	6.57±3.56	6.89±2.56**
Vitamin A (μmol/L)	0.60±0.12	0.64±0.17	0.57±0.14	0.68±0.34	0.58±0.12	0.52±0.14
Vitamin E (μmol/L)	11.2±4.14	10.8±3.11	11.1±3.40	12.3±5.02	10.9±3.96	9.32±4.38
Lycopene (mmol/L)	0.16±0.04	0.19±0.08	0.20±0.08	0.16±0.07	0.18±0.08	0.17±0.05
β-carotene (mmol/L)	0.51±0.24	0.39±0.15*	0.32±0.14**	0.24±0.14**	0.26±0.09**	0.34±0.12*

Values are means ± SD.
†One way ANOVA model
‡ number of the components of the MS that are present in participants
*: p<0.05 compared with group 0, b: p<0.01

Table 4. Associations between quartiles of serum antioxidants, MDA and the MS (OR (95%CI)) †

	Quartiles of serum composition			
	Q1	Q2	Q3	Q4
SOD	≤41.7	41.9-48.7	48.7-54.7	≥54.85
OR	1	1.22 (0.752-1.97)	0.514 (0.314-0.816)*	0.545 (0.331-0.899)*
Adjusted OR ‡	1	0.978 (0.655-1.77)	0.505 (0.302-0.844)*	0.506 (0.303-0.844)*
GSH	≤76.6	77.3-87.5	87.5-101	≥101
OR	1	0.849 (0.522-1.42)	1.27 (0.777-2.08)	0.786 (0.474-1.31)
Adjusted OR ‡	1	0.921 (0.554-1.53)	1.31 (0.794-2.16)	0.825 (0.490-1.39)
MDA	≤4.00	4.12-5.83	5.88-7.71	≥7.78
OR	1	1.073 (0.646-1.78)	1.09 (0.660-1.80)	1.74 (1.06-2.86)
Adjusted OR‡	1	1.019 (0.634-1.78)	1.03 (0.620-1.73)	1.580 (0.938-2.53)
Vitamin A	≤0.500	0.504-0.587	0.588-0.675	≥0.677
OR	1	0.875 (0.318-2.41)	0.766 (0.278-2.11)	0.875 (0.318-2.41)
Adjusted OR‡	1	0.880 (0.319-2.43)	0.760 (0.274-2.11)	0.855 (0.305-2.40)
Vitamin E	≤9.11	9.12-12.4	12.5-15.5	≥15.5
OR	1	0.438 (0.154-1.24)	0.875 (0.318-2.41)	1.51 (0.538-4.24)
Adjusted OR‡	1	0.439 (0.154-1.25)	0.876 (0.315-2.44)	1.58 (0.546-4.54)
Lycopene	≤0.112	0.113-0.165	0.167-0.226	≥0.229
OR	1	0.510 (0.183-1.42)	1.32 (0.469-3.72)	0.510 (0.183-1.42)
Adjusted OR‡	1	0.528 (0.185-1.51)	1.40 (0.468-4.16)	0.540 (0.177-1.65)
β-carotene	≤0.176	0.179-0.273	0.278-0.398	≥0.402
OR	1	0.490 (0.170-1.41)	0.429 (0.149-1.24)	0.156 (0.051-0.480)**
Adjusted OR‡	1	0.304 (0.084-1.11)	0.279 (0.079-0.978)*	0.097 (0.026-0.374)**

SOD indicates superoxide dismutase; MDA, malondialdehide; GSH-Px, glutathione peroxidase.
† Values are OR from logistic regression model, *95%CI*: confidence interval, *: $p < 0.05$, **: $p < 0.01$.
‡ Adjusted for age (25–34, 35–44,45–54, 55–64, 65–74 and 75+) and sex (male and female).

Table 5. Dietary intake of control and the MS participants

	Control Group	MS Group	p †
Energy (kcal)	1844±608	1676±572	0.004
Protein (g)	59.1±27.8	53.7±27.0	0.110
Fat (g)	71.8±31.5	79.4±37.1	0.018
Carbohydrate (g)	220±87.8	201±77.5	0.022
Protein, % of energy	12.7±3.52	12.4±3.50	0.479
Fat, % of energy	38.0±11.1	39.4±10.2	0.191
Carbohydrates, % of energy	48.9±11.2	48.0±9.96	0.382
Fiber (g)	7.18±4.34	7.65±8.75	0.245
Vitamin A (μg RE)	244±182	240±176	0.25
Vitamin E (mg)	45.7±23.1	45.1±22.6	0.60
Vitamin C (mg)	62.0±47.5	53.2±41.5	0.05
Zn (mg)	8.01±3.37	7.22±2.80	0.05
Se (μg)	43.1±30.7	38.4±25.7	0.08
Cu (mg)	1.60±0.80	1.40±0.63	0.04
Mn (mg)	4.02±1.76	3.68±2.27	0.30

Values are means ± SD. Zn indicates zinc; Se, selenium; Cu, copper; Mn, magnum.
† Multivariable linear regression model adjusting for potential cofounders including: age (25–34, 35–44, 45–54, 55–64, 65–74 and 75+) and sex (male and female)

manganese also decreased with the increasing number of the MS components (as shown in Table 6).

The associations between quartiles of dietary antioxidant nutrients intake and presence of the MS are presented in table 7. We found a lower risk of developing the MS in the second, third, and highest quintile of zinc intake with respect to the lowest quintile. The ORs for manganese intake were 0.595, 0.515, 0.474 (95% CI: 0.360-0.983, 0.309-0.856, 0.285-0.790) respectively for the second, third, highest versus the lowest quintile of intake.

When analyzing the correlations between dietary nutrients intakes and serum antioxidant status of the MS patients (Table 8), statistically significant negative correlations between antioxidant status in serum and dietary fat, energy, and protein intake were investigated. A positive association between antioxidant state and vitamin C intake was found.

DISCUSSION

Oxidative stress is a common risk factor for the pathogenesis of the MS components. In this case-control study, we aimed to investigate the associations between dietary antioxidants intake, serum oxidative level, and the risk of the MS. The present study showed significantly that serum β- carotene level and SOD activity, dietary zinc and manganese intake, was inversely related to MS.

It is well known that the main pathogenic mechanism underlying the MS relies on insulin resistance, which is promoted by oxidative stress, and may in turn aggravate the degree of oxidative status further.[18] Several studies consistently reveal the relations between oxidative stress status and inflammatory biomarkers through the action of transcription factor nuclear factor-κB.[19]

The mechanisms by which the MS components could enhance oxidative stress were suggested. The elevated levels of fatty acids in accumulated fat of abdominal obesity was associated with higher nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity and increased systemic oxidative status.[12] In this study, we used the criteria which were suggested by the IDF and require central obesity as the major component for the MS. Hyperglycemia, low HDL-C level and hypertension also may further enhance oxidative stress by stimulating the production of reactive oxygen species, and attenuating antioxidant activity.[20-22]

Table 6. Mean dietary antioxidative intakes by the MS components among participants †

	Number of the MS components in participants ‡					
	0 (*n*=74)	1 (*n*=142)	2 (*n*=59)	3 (*n*=140)	4 (*n*=66)	5 (*n*=19)
Vitamin A (μg RE)	260±181	223±178	208±160	228±176	217±131	238±143
Vitamin E (mg)	48.7±25.5	44.6±22.8	46.2±24.0	44.7±20.9	47.2±24.2	39.9±15.2*
Vitamin C (mg)	68.8±51.9	61.2±46.9	55.3±48.8	50.6±37.5*	56.9±38.4	58.4±50.3
Zn (mg)	8.0±3.4	7.9±3.3	7.1±2.9	7.1±2.9	7.7±3.4	6.1±2.4*
Se (μg)	37.1±22.2	44.0±34.0	37.4±24.9	39.9±29.1	41.9±29.0	31.0±18.8
Cu (mg)	1.5±0.6	1.6±0.9	1.3±0.5	1.4±0.7	1.4±0.62	1.1±0.5*
Mn (mg)	4.1±1.9	3.9±1.9	3.4±1.3	3.9±2.2	3.8±2.5	2.8±1.4*

Values are means ± SD. Zn indicates zinc; Se, selenium; Cu, copper; Mn, magnum.
† One way ANOVA model
‡ number of the components of the MS that are present in participants
* $p<0.05$ compared with group 0

Table 7. Associations between quartiles of dietary antioxidant nutrients intake and the MS (OR (95%CI))†

	Quartiles of intake			
	Q1	Q2	Q3	Q4
Vitamin A‡	≤106	106-182	182-314	≥316.96
OR	1	1.14 (0.681-1.86)	0.904 (0.537-1.48)	1.26 (0.751-2.05)
Adjusted OR§	1	1.31 (0.754-2.11)	0.995 (0.591-1.67)	1.31 (0.781-2.19)
Vitamin E‡	≤29.7	29.7-42.9	43.0-58.0	≥58.2
OR	1	0.619 (0.375-1.02)	0.853 (0.527-1.42)	0.626 (0.379-1.04)
Adjusted OR§	1	0.649 (0.373-1.04)	0.854 (0.514-1.413)	0.619 (0.370-1.04)
Vitamin C‡	≤26.9	27.1-44.8	45.00-79.19	≥79.54
OR	1	0.738 (0.443-1.23)	0.600 (0.364-1.019)	0.622 (0.372-1.04)
Adjusted OR§	1	0.770 (0.456-1.30)	0.626 (0.369-1.060)	0.628 (0.371-1.06)
Zinc‡	≤5.80	5.81-7.19	7.19-9.34	≥9.34
OR	1	0.354 (0.217-0.593)**	0.372 (0.225-0.617)**	0.186 (0.108-0.318)**
Adjusted OR§	1	0.332 (0.198-0.556)**	0.336 (0.200-0.565)**	0.181 (0.104-0.315)**
Selenium ‡	≤22.0	22.1-32.3	32.38-50.49	≥50.69
OR	1	1.41 (0.863-2.31)	0.944 (0.581-1.57)	0.811 (0.490-1.34)
Adjusted OR§	1	1.38 (0.890-2.45)	0.806 (0.540-1.49)	0.819 (0.464-1.30)
Copper‡	≤1.05	1.05-1.32	1.32-1.84	≥1.85
OR	1	0.768 (0.463-1.24)	0.675 (0.406-1.09)	0.579 (0.345-0.941)*
Adjusted OR§	1	0.751 (0.454-1.24)	0.646 (0.389-1.07)	0.605 (0.364-1.01)
Magnum ‡	≤2.62	2.62-3.38	3.39-4.56	≥4.56
OR	1	0.598 (0.370-0.992)*	0.525 (0.320-0.863)*	0.459 (0.278-0.758)**
Adjusted OR§	1	0.595 (0.360-0.983)*	0.515 (0.309-0.856)*	0.474 (0.285-0.790)*

† Values are OR from logistic regression model, * $p < 0.05$, ** $p <0.01$.
‡ All antioxidant nutrients intakes were adjusted for energy intake by the regression residual method.[17]
§ Adjusted for age (25–34, 35–44, 45–54, 55–64, 65–74 and 75+) and sex (male and female)

The data from our study presented that MS subjects had lower SOD and β- carotene, and higher MDA, which is a lipid peroxide product. The SOD contains redox metals in the catalytic center which can dismutase superoxide radicals to hydrogen peroxide and oxygen.[23] The antioxidant actions of β-carotene are based on their singlet oxygen quenching properties and their ability to trap peroxyl radicals and to convert into retinoids in the human body.[23] These findings are consistent with data reported by Isogawa *et al.*[24] who indicated serum T-SOD activity was positively correlated with the components of MS. Armutcu *et al.*[25] reported that subjects with MS had significantly higher lipid peroxide concentrations, which was in accordance with our finding. Also in our study, we demonstrated increasing concentrations of β-carotene and SOD in serum with decreasing prevalence of MS as shown in table 4. It is noteworthy that we found that the number of MS components inversely correlates with serum SOD, GSH-Px, and β-carotene. It appears that antioxidants, such as SOD and β-carotene, could be one of the factors to attenuate the development of MS.

As demonstrated in Table 5, MS patients had a lower energy and carbohydrate, but higher total fat intake compared with control participants. In contrast to our finding, other studies found that higher fat and carbohydrate intake were associated with increased odds of the MS.[26,27] It may be responsible for this phenomenon that patients with the MS components in our study may have changed their dietary habits based their nutritional knowledge, but not the adequate dietary guidelines. And the proportions of dietary energy from macronutrients weren't significantly different between these two groups. It may be illuminated by the large random variation in these proportions. Dietary antioxidants status may exert powerful influences on the degree of injury caused by oxidative stress. The free radical self- amplifying chain reaction can be broken by vitamin C, which also acts as a key cofactor for several enzymes catalyzing hydroxylation reactions.[28]

Table 8. Correlation coefficients for the association between dietary intakes and composition of serum antioxidants and MDA in the MS participants †

	dietary intake											
Serum assessments	Fat	Energy	Protein	Carbohydrate	Fiber	Zn	Se	Vitamin A	Vitamin E	Vitamin C	Cu	Mn
Vitamin A *r*	0.095	0.105	0.121	0.069	0.007	0.157	0.207*	-0.037	0.103	-0.062	0.073	0.021
Partial *r* ‡	0.116	0.109	0.135	0.065	-0.020	0.054	0.284*	-0.088	0.132	-0.070	0.121	-0.040
Vitamin E *r*	0.011	-0.047	-0.069	-0.066	0.128	-0.110	0.102	0.007	0.069	-0.028	-0.048	0.065
Partial *r* ‡	-0.010	-0.084	-0.142	-0.100	0.058	-0.128	0.006	0.086	0.126	-0.026	-0.000	0.083
Lycopene *r*	-0.160	-0.262*	-0.302*	-0.226*	-0.101	-0.319*	-0.074	-0.042	-0.035	0.076	-0.107	0.084
Partial *r* ‡	-0.202	-0.236*	-0.247*	-0.179	-0.129	-0.256*	-0.040	0.082	0.033	-0.120	-0.133	-0.086
β-carotene *r*	0.077	-0.046	-0.091	-0.108	-0.093	-0.115	-0.034	-0.103	0.070	-0.053	-0.091	-0.071
Partial *r* ‡	0.056	0.007	0.019	-0.047	-0.029	-0.012	0.014	0.014	0.129	-0.050	-0.076	-0.009
SOD *r*	-0.102	-0.146*	-0.113	-0.127	0.054	0.026	-0.047	0.024	0.025	0.060	0.062	0.023
Partial *r* ‡	-0.078	-0.144*	-0.085	-0.118	0.082	0.019	-0.068	0.031	0.045	0.076	0.033	-0.003
GSHPX *r*	-0.024	-0.025	0.003	-0.009	-0.045	-0.005	0.027	0.055	-0.016	0.013	-0.016	0.039
Partial *r* ‡	-0.038	-0.047	-0.012	-0.048	-0.027	-0.018	0.008	0.068	0.014	0.005	-0.014	0.043
MDA *r*	0.150*	0.218*	0.158*	0.109	0.010	0.120	-0.028	0.077	0.040	-0.143*	0.135	0.034
Partial *r* ‡	0.193*	0.213*	0.148*	0.119	-0.009	0.108	-0.019	0.076	0.025	-0.142*	0.141	0.039

SOD, superoxide dismutase; MDA, malondialdehide; GSH-Px, glutathione peroxidase.
† Values are Correlation coefficients from Pearson correlation model or partial correlation model, * $p<0.05$
‡ Controlled for age (25-34, 35-44,45-54, 55-64, 65-74 and 75+) and sex (male and female).

Zinc and copper are essential constituents of SOD,[24] and zinc is also an inhibitor of NF-κB which is activated by oxidative stress, and an O^{2-} synthesis enzyme named NADPH oxidase.[29] In addition to its antioxidant property, zinc is involved in the synthesis, storage, and release of insulin.[30] In the present study, dietary vitamin C, zinc, and copper intakes of the MS patients were lower than those of the control group. Dietary total antioxidant capacity (TAC) showed positive and significant associations with vitamins A and C, magnesium, selenium, and zinc intakes. Dietary total antioxidant capacity is negatively associated with some MS features in healthy young adults. So our data indicated that dietary TAC of the MS patients may be lower compared to the control group. Our findings regarding dietary antioxidant intakes were supported by a previous study in which dietary TAC was negatively associated with most components of the MS,[31] and an inverse association between dietary zinc intake and the MS was presented in our study as shown in table 7. We found the role of dietary zinc status independent of the effects of energy intake which was adjusted in our logistic model. There was a 4-week oral zinc supplementation trial among prepubescent children with the MS, in which zinc supplement led to weight loss.[32] Considering the essential roles that zinc plays in antioxidant systems and insulin sensitivity, our results stressed the protective effect of dietary zinc intake on the MS. Our findings displayed that higher dietary zinc intake may be associated with lower risk of the MS.

In this study, we investigated the correlations between dietary intakes and circulating levels of antioxidant status in the MS patients. Negatively significant correlation coefficients were observed between dietary fat, energy, protein intake and serum antioxidant state. There was a study[33] that showed that fatty meals led to higher postprandial oxidative stress. Antioxidant enzymes induced by excess energy in the form of high-fat, high-protein animal meals are not sufficient to block oxidative stress. This may be the mechanism underlying our data of association of dietary and serum antioxidant level. As for the negative correlation coefficient between dietary zinc intake and serum lycopene level, a possible explanation for this phenomenon may be the more consumption of animal foods which were high in zinc and low in lycopene. However, comparison of associations between dietary and serum antioxidants is difficult, because the bioavailability of dietary nutrients were influenced by factors such as characteristics of the food source, interactions with other dietary factors, cooking conditions, and various subject characteristics. Besides these mechanisms, vitamins A, E, and β-carotene are liposoluble, and may be accumulated in adipose tissue. So differences in dietary liposoluble antioxidants may not be directly reflected in serum antioxidants.

There are several potential limitations in the present study. First, due to the cross-sectional design, this study can only evaluate associations but not definitive causation. Second, we did not measure participants' physical activity, which was a potential confounder. Third, we got participants' temporal dietary information via 3 day food records, which could partly interpret inconsistency of serum status and dietary antioxidants intake. Furthermore, we did not exclude the MS patients who have accepted therapy, and that would affect the association between serum assessment and MS.

In conclusion, higher serum SOD and β-carotene level, and less dietary intake of energy, and fat may reduce the risk for the MS. Meanwhile, this study revealed a negative association between serum antioxidant status and dietary fat, energy, protein, and zinc intake in the MS patients, and there was a positive association between serum antioxidant state and dietary intake of vitamin C. These findings suggest that higher antioxidant and lower fat and energy intake could beneficially affect serum oxidative status, followed by attenuating MS.

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AUTHOR DISCLOSURES

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REFERENCES

1. Maury E, Brichard SM. Adipokine dysregulation, adipose tissue inflammation and metabolic syndrome. Mol Cell Endocrinol. 2010;314:1-16.
2. Grundy SM. Metabolic syndrome pandemic. Arterioscler Thromb Vasc Biol. 2008;28:629-36.
3. Suzuki A, Kosuge K, Nanyu O. Five year study of cardiovascular risk factors in Japanese people: implications concerning new onset of metabolic syndrome. Intern Med. 2010; 49:1-6.
4. Roberts CK, Sindhu KK. Oxidative stress and metabolic syndrome. Life Sci. 2009;84:705-12.
5. Hopps E, Noto D, Caimi G, Averna MR. A novel component of the metabolic syndrome: The oxidative stress. Nutr Metab Cardiovasc Dis. 2010;20:72-7.
6. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns, insulin resistance, and prevalence of the metabolic syndrome in women. Am J Clin Nutr. 2007;85:910-8.
7. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Fruit and vegetable intakes, C-reactive protein, and the metabolic syndrome. Am J Clin Nutr. 2006;84: 1489-97.
8. Ford ES, Mokdad AH, Giles WH, Brown DW. The metabolic syndrome and antioxidant concentrations: findings from the Third National Health and Nutrition Examination Survey. Diabetes. 2003;52:2346-52.
9. Yoo S, Nicklas T, Baranowski T, Zakeri IF, Yang S, Srinivasan SR, et al. Comparison of dietary intakes associated with metabolic syndrome risk factors in young adults: the Bogalusa Heart Study. Am J Clin Nutr. 2004;80: 841-8.
10. Djoussé1 L, Padilla1 H, Nelson TL, Gaziano JM, Mukamal KJ. Diet and metabolic syndrome. Endoc Metab Immune Disord Drug Targets. 2010;10:124-37.
11. Sugiura M, Nakamura M, Ogawa K. Associations of serum carotene concentrations with the metabolic syndrome: interaction with smoking. Br J Nutr. 2008;100:1297-306.
12. Skalicky J, Muzakova V, Kandar R, Meloun M, Rousar T, Palicka V. Evaluation of oxidative stress and inflammation in obese adults with metabolic syndrome. Clin Chem Lab Med. 2008;46:499-505.
13. Demirbag R, Yilmaz R, Gur M, Celik H, Guzel S, Selek S,

et al. DNA damage in metabolic syndrome and its association with antioxidative and oxidative measurements. Int J Clin Pract. 2006;60:1187-93.
14. Fujita K, Nishizawa H, Funahashi T, Shimomura I, Shimabukuro M. Systemic oxidative stress is associated with visceral fat accumulation and the metabolic syndrome. Circ J. 2006;70:1437- 42.
15. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/ National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112:2735-52.
16. Friedewald WT, Levy R, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without the use of the preparative ultracentrifuge. Clin Chem. 1972;18:499-502.
17. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. Am J Clin Nutr. 1997;65:S1220-8.
18. Paolisso G, Tagliamonte MR, Rizzo MR, Giugliano D. Advancing age and insulin resistance: new facts about an ancient history. Eur J Clin Invest. 1999;29:758-69.
19. Koh KK, Oh PC, Quon MJ. Does reversal of oxidative stress and inflammation provide vascular protection? Cardiovasc Res. 2009;81:649-59.
20. Lee KU. Oxidative stress markers in Korean subjects with insulin resistance syndrome. Diabetes Res Clin Pract. 2001; 54: S29-33.
21. Abdilla1 N., Tormo MC., Fabia1 MJ, Chaves FJ, Saez G, Redon J. Impact of the components of metabolic syndrome on oxidative stress and enzymatic antioxidant activity in essential hypertension. J Hum Hypertens. 2007;21:68-75.
22. Hansel B, Giral P, Nobecourt E, Chantepie S, Bruckert E, Chapman J, et al. Metabolic syndrome is associated with elevated oxidative stress and dysfunctional dense highdensity lipoprotein particles displaying impaired antioxidative activity. J Clin Endocrinol Metab. 2004;89:4963-71.
23. Paiva SA, Russell RM. β-Carotene and other carotenes as antioxidants. J Am Coll Nutr. 1999;18:426-33.
24. Isogawa A, Yamakado M, Yano M. Shiba T. Serum superoxide dismutase activity correlates with the components of metabolic syndrome or carotid artery intima-media thickness. Diabetes Res Clin Pract. 2009;86:213-8.
25. Armutcu F, Ataymen M, Atmaca H, Gurel A. Oxidative stress markers, C-reactive protein and heat shock protein 70 levels in subjects with metabolic syndrome. Clin Chem Lab Med. 2008;46:785-90.
26. Chen X, Pang Z, Li K. Dietary fat, sedentary behaviors and the prevalence of the metabolic syndrome among Qingdao adults. Nutr Metab Cardiovasc Dis. 2009;19:27-34.
27. Park Y, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. Arch Intern Med. 2003;163:427-36.
28. Young IS, Woodside JV. Antioxidants in health and disease. J Clin Pathol. 2001;54:176-86.
29. Prasad AS. Clinical, immunological, anti-inflammatory and antioxidant roles of zinc. Exp Gerontol. 2008;43:370-7.
30. Brand-Neto J, Silva CAB, Figueiredo NB, Shuhama T, Holanda MBS, Diniz JMM. Zinc kinetics in insulin-dependent diabetes mellitus patients. Biometals. 2000;13: 141-5.
31. Puchau B, Zule A, Echavarri A, Hermsdorff HHM, Martinez JA. Dietary total antioxidant capacity is negatively associated with some metabolic syndrome features in healthy young adults. Nutrition. 2010;26:534-41.
32. Kelishadi R, Hashemipour M, Adeli K, Tavakoli N, Movahedian-Attar A, Shapouri J, et al. Effect of Zinc Supplementation on Markers of Insulin Resistance, Oxidative Stress, and Inflammation among Prepubescent Children with Metabolic Syndrome. Metab Syndr Relat Disord. 2010;8:505-10.
33. Devaraja S, Wang-Polagrutob J, Polagruto J, Keen CL, Jialal I. High-fat, energy-dense, fast-food–style breakfast results in an increase in oxidative stress in metabolic syndrome. Metabolism. 2008;57:867-70.

Original Article

Serum and dietary antioxidant status is associated with lower prevalence of the metabolic syndrome in a study in Shanghai, China

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中国上海关于血清和膳食抗氧化状态与低代谢综合征患病率相关的研究

目的：本研究是为了探讨代谢综合征与血清抗氧化状态之间的关系。方法：此次研究为横断面调查，共包含年龄在 18 至 65 岁的 221 名代谢综合征患者和 329 名对照人群。检测调查对象的体重、身高、体质指数、超氧化物歧化酶、谷胱甘肽过氧化酶、丙二醛、维生素 A、维生素 E、β-胡萝卜素和番茄紅素。同时，还计算膳食中抗氧化物质的摄取情况。结果：校正年龄、性别之后，与对照组相比，代谢综合征患者超氧化物歧化酶、β-胡萝卜素浓度较低，丙二醛含量较高（p<0.05）。代谢综合征的组分数量增加时，超氧化物歧化酶、谷胱甘肽过氧化酶、β-胡萝卜素含量随之降低（p<0.05）。血清低超氧化物歧化酶、β-胡萝卜素与代谢综合征相关。另外，代谢综合征组膳食能量、碳水化合物、维生素 C、锌、铜摄入相对较低，而脂质摄入较高。膳食维生素 E、维生素 C、镁的摄入随之代谢综合征组分数量增加而降低。并且与第一四分位数组相比，锌和镁的其他四分位数组的代谢综合征风险降低。在代谢综合征患者中，膳食脂质、总能量摄入与血清抗氧化水平呈负相关，而维生素 C 摄入与血清抗氧化水平呈正相关。结论：血清抗氧化水平与低患病风险相关，也与膳食中脂肪、能量低摄入和高维生素 C 摄入相关。

關鍵字：人類、抗氧化、血清、膳食、代谢综合征