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Association between the oxidative balance score with metabolic syndrome traits in US adults

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Abstract

Objective To explore the association between the Oxidative Balance Score (OBS), which represents the balance of multiple oxidative stress-related dietary and lifestyle exposures, and the risk of metabolic syndrome (MetS).

Methods A population-based cross-sectional study design was adopted and 16,850 participants in NHANES database were included in the statistics analysis stage. The OBS was constructed by combining information from 20 a priori selected pro- and antioxidant factors. Weighted logistic regression and restricted cubic splines (RCS) were used to estimate the association between OBS and MetS.

Results Participants in the highest OBS quartile, indicating low oxidative stress (OS) levels, exhibited a significantly lower risk of MetS (odds Ratio [OR] = 0.55, 95% confidence Interval [CI]: 0.47–0.64) compared to the lowest quartile. Specifically, higher OBS was inversely associated with abdominal obesity (OR = 0.61, 95% CI: 0.54–0.69), hypertension (OR = 0.69, 95% CI: 0.58–0.83), elevated triglycerides (OR = 0.68, 95% CI: 0.57–0.82), low high-density lipoprotein cholesterol (HDL-C) levels (OR = 0.60, 95% CI: 0.50–0.70) and fasting blood glucose (FBG) levels (OR = 0.74, 95% CI: 0.62–0.88). The observed inverse association between OBS and hypertension or FBG levels appeared to primarily influenced by BMI. The association between dietary OBS intervals and elevated FBG levels was not statistically significant in men, whereas the risk was lower by 25% in women.

Conclusions A higher OBS, representing a balance of multiple oxidative stress-related dietary and lifestyle exposures, is associated with a lower risk of MetS. Therefore, adhering to an antioxidant diet and lifestyle may help prevent the occurrence of metabolic disorders.

Keywords Oxidative Balance Score, Metabolic Syndrome, Fasting blood glucose, Dietary, Lifestyle

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Introduction

Metabolic syndrome (MetS) is a state of metabolic abnormalities or metabolic disorders, characterized by a collection of risk factors affecting the onset of cardiovascular disease and type II diabetes, specifically manifested as hypertension, hyperglycemia, dyslipidemia and abdominal obesity [1, 2]. The prevalence of MetS varies among different ethnic groups, and MetS can affect approximately 10–50% of adults worldwide [3]. According to recent data published by the Centers for Disease Control and Prevention (CDC), in the United States, approximately 36.6% of adults suffer from MetS [4], and the condition is also prevalent among younger populations [5]. Since MetS and its components can affect a variety of diseases and overall mortality [6, 7], it has become a critical hidden threat to human health and a huge burden affecting the national economy.

MetS emerges as a complex interplay of multiple factors, encompassing detrimental dietary patterns and poor lifestyles as contributing elements [4]. Studies have supported that oxidative stress (OS) may play a crucial role in the occurrence and development of MetS [8, 9]. OS refers to the disruption of the delicate balance between prooxidants and antioxidants, resulting in an upregulation of reactive nitrogen oxides (RONS) and subsequent damage to macromolecules such as lipids, proteins, and DNA. This ultimately leads to cellular injury and perturbation of redox signaling pathways [10]. Alcohol, in its effects, serves as an OS inducer by inhibiting antioxidant enzymes and inciting inflammatory responses [11]. In addition to a pro-oxidative lifestyle, diet-related nutrients also affect the level of OS in the body. There is growing evidence that high intakes of nutrients such as vitamin C [12], vitamin D [13], and calcium [14] can protect against OS. In vitro experiments have shown that certain antioxidant nutrients, such as vitamin E and selenium, can reverse OS-induced inflammatory responses [15]. These studies highlight the role of free radical-mediated OS in contributing to manifestations of MetS, such as abdominal obesity, hyperlipidemia, and hypertension [16]. Notably, in vitro evidence suggests that antioxidants have the potential to decelerate these processes. However, when it comes to human studies, particularly clinical trials, the results have been less promising. Antioxidants as preventive agents have often yielded ineffective or even adverse outcomes [17, 18]. Bahadoran et al. noted that combinations of multiple antioxidant nutrients were more strongly associated with metabolic abnormalities than any single antioxidant component [19]. Because pro- and anti-oxidant factors may be interrelated and interact with each other, assessing the independent association of a single factor on individual exposure cannot provide a comprehensive picture of its role in the overall oxidative balance reaction. To address this issue, an oxidative balance score (OBS) was developed by Van Hoydonck et al. in Belgium (2002) and used as a measure of the combined assessment of pro- and anti-oxidant exposure, with higher OBS indicating lower oxidative stress response [20–23]. However, the epidemiological research on the association between OBS and the presence of MetS and its components is both limited and yields contradictory results [24, 25].

Considering the role of OS in the occurrence and development of MetS, the purpose of this study was to construct OBS by combining dietary components and lifestyle in a large sample nationally representative cohort of the United States, and to explore its influence on the risk of MetS and its components.

Materials and methods

Study population

The National Health and Nutrition Examination Survey (NHANES) stands as a pivotal, nationally representative cross-sectional survey of the civilian, non-institutionalized U.S. population, conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) [26]. The survey employs a sophisticated, multi-stage and probability sampling design, systematically enrolling an annually refreshed cohort of approximately 5,000 individuals since 1999. Integral data collection takes place through comprehensive health interviews and meticulous physical examinations, culminating in a biennial dissemination of findings. The study protocol of NHANES has been approved by the Research Ethics Review Committee of the NCHS, and each participant has provided written informed consent before participating in the study [27].

This study initially included 32,464 subjects over the age of 20 who participated in NHANES from 1999 to 2010, and individuals were excluded if (1) they were pregnant (n=1299), (2)they lost data for any of the MetS components (n=3291), (3) they lost data for any of the OBS components (n=9469), (4) they lost data for any of the covariates (n=1552), (5) they lost data for any of the C-reactive protein (CRP) (n=3). Finally, a total of 16,850 participants were included in the analysis.

Determination of MetS and its components

According to the National Cholesterol Education Adult Treatment Group-III standard [28], MetS diagnosis requires the presence of two or more of the following disorders:

(1) Hyperglycemia, indicated by a fasting blood glucose (FBG) level ≥ 100 mg/dL (5.6 mmol/L) or the use of antidiabetic medications;
(2) Reduced high-density lipoprotein cholesterol (HDL-C) levels, with < 40 mg/dL (1.04 mmol/L) for men

and < 50 mg/dL (1.29 mmol/L) for women, or the administration of lipid-lowering medications;
(3) Hypertriglyceridemia, identified by a triglyceride (TG) level ≥ 150 mg/dL (1.69 mmol/L);
(4) Abdominal obesity, defined as a waist circumference (WC) of ≥ 102 cm for men and ≥ 88 cm for women;
(5) Hypertension, denoted by systolic/diastolic blood pressure ≥ 130/85mmHg or the use of antihypertensive medications.

Variable collection and measurement

Both dietary and lifestyle components were used in the calculation of OBS. Dietary energy intake data were acquired through 24-hour dietary recall interviews (24 h) conducted. The assessment of dietary nutrient intake was conducted utilizing the University of Texas Food Intake Analysis System, in conjunction with the U.S. Department of Agriculture Survey Nutrient Database. Drinking habits were ascertained from the 24 h interviews. Smoking status as reflected by serum cotinine levels. Body mass index (BMI) was derived by dividing an individual's weight in kilograms by the square of their height in meters (kg/m^2). Additionally, participants' weekly metabolic equivalent (MET) values were calculated based on specific leisure activities undertaken in the preceding 30 days, with pertinent details sourced from family interviews.

In this study, covariates were certain factors hypothesized to be associated with MetS or OBS, including age, gender, race, educational attainment, marital status, and poverty-to-income ratio (PIR). To estimate dietary energy intake, we computed the mean of data gathered from interviews conducted on both day 1 and day 2. For quantification of C-reactive protein (CRP) concentrations, we employed latex-enhanced nephelometry using the Dade Behring Nephelometer II analyzer system (Dade Behring Diagnostics Inc., Somerville, NJ).

OBS components and assessment methods

The calculation of the OBS entailed an evaluation of 16 nutrients and 4 lifestyle factors, encompassing a total of 5 pro-oxidants and 15 antioxidants. These selections were guided by a priori insights into the interplay between oxidative stress (OS) and these specific nutrients or lifestyle attributes [21, 29].

These components were divided into four distinct categories:

(1) Dietary antioxidants: This category encompassed dietary fiber, carotene, riboflavin, niacin, vitamin B6, total folic acid, vitamin B12, vitamin C, vitamin E, calcium, magnesium, zinc, copper, and selenium. For dietary antioxidants, we categorized the participants into three groups based on their tertiles. The lowest tertile group awarded 0 points, the middle tertile group awarded 1 points, and the highest tertile group awarded 2 points.
(2) Dietary prooxidants comprising iron and total fat, this group provided insights into dietary prooxidant effects. Notably, for dietary prooxidants, we employed a scoring distribution that was inverse to that of the other categories—awarding 0 points to the highest tertile, 1 points to the middle tertile group and 2 points to the lowest tertile.
(3) Non-dietary antioxidants: Within this grouping, the factor examined was physical activity, representing non-dietary antioxidant contribution. For the quantification of physical activity (PA), which was calculated by the formula: PA = MET × weekly frequency × duration, the lowest tertile group awarded 0 points, the middle tertile group awarded 1 points, and the highest tertile group awarded 2 points. The higher the PA score, the higher the antioxidant activity.
(4) Non-dietary prooxidants: This classification incorporated cotinine, alcohol consumption, and BMI as indicators of non-dietary prooxidant influences. The scoring distribution for non-dietary prooxidants was 0 points for the highest tertile and 2 points for the lowest tertile. Specifically, we assigned scores for alcohol consumption: 0 points for females consuming ≥ 15 g/d, males consuming ≥ 30 g/d, 1 point for females consuming 0–15 g/d, males consuming 0–30 g/d, and 2 points for non-drinkers. The dietary OBS was derived through the summation of scores attributed to the sixteen dietary factors. In contrast, the lifestyle OBS was calculated by aggregating the scores associated with the four distinct lifestyle components, as detailed in Table 1.

Statistical methods

Considering complex sampling survey designs according to the NHANES analysis guidelines and incorporating appropriate sample weights to account for the differential probability of selection, allowed extrapolation of research results to the U.S. adult population. Continuous variables were presented as weighted means and standard errors or medians with interquartile ranges, and categorical variables were presented as numerical values and weighted percentages. The differences between continuous and categorical variables in each OBS group were evaluated using weighted Wald-F and Rau-Scott chi-square tests.

Weighted logistic regression was used to estimate the association between OBS and MetS as represented by odd ratio (OR) and 95% confidence interval (CI). OBS was used as a continuous variable to judge whether there

Table 1 Score allocation scheme for each component of OBS

OBS components	Male			Female		
	0	1	2	0	1	2
Dietary fiber (g/d) [A]	<=12.30	12.31–20.20	> 20.20	<=10.10	10.11–16.50	> 16.50
Carotene (RE/d) [A]	<=41.25	41.26-146.46	> 146.46	<=37.94	37.95-159.68	> 159.68
Riboflavin (mg/d) [A]	<=1.76	1.77–2.70	> 2.70	<=1.34	1.35–2.07	> 2.07
Niacin (mg/d) [A]	<=20.83	20.84–31.73	> 31.73	<=14.61	14.62–22.48	> 22.48
Vitamin B6 (mg/d) [A]	<=1.59	1.60–2.50	> 2.50	<=1.14	1.15–1.80	> 1.80
Total Folate (mcg/d) [A]	<=317.00	317.01–501.00	> 501.00	<=244.15	244.16–384.00	> 384.00
Vitamin B12 (mcg/d) [A]	<=3.35	3.36–6.39	> 6.39	<=2.29	2.30–4.49	> 4.49
Vitamin C (mg/d) [A]	<=36.00	36.01–107.40	> 107.40	<=32.60	32.61–93.53	> 93.53
Vitamin E (ATE) (mg/d) [A]	<=5.50	5.51–10.08	> 10.08	<=4.46	4.47–8.08	> 8.08
Calcium (mg/d) [A]	<=648.00	648.01–1103.00	> 1103.00	<=537.00	537.01–906.00	> 906.00
Magnesium (mg/d) [A]	<=249.00	249.01–364.00	> 364.00	<=192.00	192.01–282.00	> 282.00
Zinc (mg/d) [A]	<=9.42	9.43–15.17	> 15.17	<=6.89	6.90-10.79	> 10.79
Copper (mg/d) [A]	<=1.06	1.07–1.59	> 1.59	<=0.83	0.84–1.25	> 1.25
Selenium (mcg/d) [A]	<=93.70	93.71–143.70	> 143.70	<=67.80	67.81–102.20	> 102.20
Total Fat (mg/d) [P]	> 106.45	66.50-106.45	<=66.49	> 77.3	48.88–77.3	<=48.87
Iron (mg/d) [P]	> 19.36	12.54–19.36	<=12.53	> 14.44	9.48–14.44	<=9.47
Physical activity [A]	<=378.00	378.01–1890.00	> 1890.00	<=320.00	320.01–1200.00	> 1200.00
Alcohol (g/d) [A]	> 30.00	0.00–30.00	None	> 15.00	0.00–15.00	None
BMI (kg/m^2) [A]	> 29.66	25.64–29.66	<=25.63	> 30.47	24.76–30.47	<=24.75
Cotinine (ng/mL) [A]	> 2.52	0.05–2.52	<=0.04	> 0.16	0.02–0.16	<=0.01

OBS indicates oxidative balance score; A, antioxidant; P, prooxidant; RE, retinol equivalent; ATE, alpha-tocopherol equivalent; BMI, body mass index

was a nonlinear relationship with MetS and OBS was used as a categorical variable to calculate the *P* value of the trend test. We constructed three models in this study. Model 1 was a rough model without adjusting any confounding factors, model 2 adjusted age, race, marital status, education level and PIR, and model 3 further adjusted the energy intake and CRP on the basis of model 2. OBS were classified into dietary OBS and lifestyle OBS to discuss their relationship with MetS traits overall and stratified by sex, separately. In addition, we conducted weighted multivariate linear regression models to evaluate the association between OBS and cardiometabolic markers. Furthermore, restricted cubic spline (RCS) regression was used to verify the relationship between MetS traits and OBS overall and stratified by sex by setting 4 knots and using logistic regression models.

Sensitivity analysis

Two sensitivity analyzes were performed in this study. Firstly, due to the slightly variable diagnostic criteria for MetS, WC, HDL-C, TG and FBG levels could be analyzed as continuous variables of MetS components to further analyze role of OBS. Secondly, a stepwise approach was taken to evaluate the influence of each individual component in the construction of OBS. By iteratively removing one component at a time, we gauged whether the resultant scores, composed of the remaining 19 factors, exerted any discernible effects on the outcomes.

All statistical analysis were performed using R version 4.2.1. The significance tests were two-tailed, and two-tailed $P<0.05$ was considered statistically significant.

Results

The distribution of the baseline characteristics and biochemical measures of the study subjects across the OBS quartiles range

The distribution of baseline characteristics and biochemical measures among the OBS quartiles are presented in Table 2. The mean age was 45.19±0.26 years, comprising 7862 (46.66%) females and 8988 (53.34%) males. Predominantly, subjects were non-Hispanic white (54.59%). All participants were categorized into four groups according to OBS quartiles: Q1 (OBS, 3 to 15), Q2 (OBS, 16 to 21), Q3 (22 to 26), and Q4 (27 to 37). Compared to the lowest OBS quartile, individuals in the highest quartile tended to have higher income levels, be more married, highly educated, elevated total energy intake and lower concentrations of CRP. Notably, gender distribution did not exhibit significant variance across OBS quartiles, thereby indicating a balanced representation of both males and females within each quartile. Moreover, differences in age distribution across OBS groups did not achieve statistical significance. As for MetS traits, with the exception of diastolic blood pressure (DBP), the distribution of other cardiometabolic characteristics (WC, FBG, TG, HDL-C and SBP) was statistically different across OBS quartiles.

Table 2 The distribution of baseline characteristics and metabolic-related factors among OBS quantiles for 16,850 participants

Characteristics	Total	Q1	Q2	Q3	Q4	*P*-value
	n **= 16,850**	***n*** **= 4640**	***n*** **= 4548**	***n*** **= 3697**	***n*** **= 3965**	
Age (Years)	45.19(0.26)	45.18(0.33)	45.73(0.35)	45.22(0.38)	44.65(0.39)	0.06
PIR	3.19(0.03)	2.82(0.05)	3.14(0.04)	3.35(0.05)	3.45(0.04)	**< 0.0001**
Energy (kcal)	2240.20(11.99)	1541.54(13.53)	2023.94(15.80)	2450.89(21.25)	2941.48(27.98)	**< 0.0001**
CRP (mg/dL)	0.37(0.01)	0.45(0.02)	0.37(0.01)	0.34(0.02)	0.29(0.01)	**< 0.0001**
Sex (%)						0.39
Female	7862(46.66)	2143(49.43)	2100(47.47)	1713(47.90)	1906(49.49)	
Male	8988(53.34)	2497(50.57)	2448(52.53)	1984(52.10)	2059(50.51)	
Race/Ethnicity (%)						**< 0.0001**
Non-Hispanic White	9199(54.59)	2219(70.40)	2431(73.72)	2168(78.72)	2381(79.96)	
Non-Hispanic Black	2924(17.35)	1147(13.64)	802(9.70)	519(6.80)	456(5.60)	
Mexican-Americans	3040(18.04)	829(6.84)	849(6.86)	638(6.27)	724(6.63)	
Other	1687(10.01)	445(9.12)	466(9.72)	372(8.21)	404(7.81)	
Marital status (%)						**< 0.0001**
Married life	10,690(63.44)	2744(61.59)	2879(63.98)	2447(67.20)	2620(68.52)	
Divorced /widowed	2781(16.5)	889(17.18)	750(14.13)	590(14.63)	552(11.95)	
Unmarried	3379(20.05)	1007(21.23)	919(21.89)	660(18.16)	793(19.53)	
Education level (%)						**< 0.0001**
Less than high school	4002(23.75)	1400(19.74)	1139(15.78)	766(12.89)	697(10.08)	
High school	4009(23.79)	1261(29.44)	1102(25.42)	855(23.99)	791(18.65)	
More than high school	8839(52.46)	1979(50.82)	2307(58.80)	2076(63.12)	2477(71.27)	
WC (cm)	96.61(0.24)	98.82(0.39))	97.54(0.32)	96.20(0.38)	93.91(0.37)	**< 0.0001**
FBG (mg/dL)	102.24(0.43)	103.49(0.76)	103.42(0.85)	101.34(0.77)	100.64(0.74)	**0.01**
TG (mg/dL)	140.42(2.06)	145.25(3.61)	145.90(4.93)	138.65(3.64)	131.71(3.79)	**0.03**
HDL-C (mg/dL)	52.73(0.23)	50.56(0.31)	52.26(0.35)	53.18(0.40)	54.88(0.36)	**< 0.0001**
SBP (mmHg)	121.31(0.22)	122.36(0.43)	122.02(0.29)	121.23(0.39)	119.67(0.36)	**< 0.0001**
DBP (mmHg)	71.66(0.22)	72.01(0.26)	71.70(0.31)	71.55(0.30)	71.38(0.32)	0.35
MetS (%)						**< 0.0001**
Without	11,993(71.18)	3123(68.68)	3171(72.17)	2674(74.13)	3025(78.59)	
With	4857(28.82)	1517(31.32)	1377(27.83)	1023(25.87)	940(21.41)	

MetS indicates metabolic syndrome; WC, waist circumference; HDL-C, high-density lipoprotein cholesterol; FBG, fasting blood glucose; TG, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; PIR, the ratio of family income to poverty; CRP, C-reactive protein

Association between OBS and MetS and its components

Table 3 shows the association between OBS as a categorical variable and a continuous variable and MetS traits. When OBS was used as a continuous variable, we found higher OBS was negatively associated with MetS both in crude model and adjusted model. After adjusted all covariables, each one SD increase in the OBS was found to be associated with an 4% decrease in the risk of MetS (OR = 0.96, 95%CI = 0.95–0.97). When OBS was used as a categorical variable and compared with the lowest quantile as a reference, the OR values of MetS in the Q4 group (the OBS group with the strongest antioxidant properties) were 0.55 (95%CI: 0.47–0.64, *P* for trend < 0.0001). Participants in the other three groups were less likely to be at risk for MetS than participants in the lowest quartile.

The results of the multivariable logistic regressions showed that OBS was significantly associated with MetS components. When OBS was treated as a continuous variable, it was significantly and negatively associated with high WC (OR = 0.96), elevated TG (OR = 0.99), low HDL-C(OR = 0.97), hypertension (OR = 0.98) and elevated FBG levels (OR = 0.98). After full adjustment, the results remained significant, the estimates of OR were 0.95, 0.98, 0.97, 0.98 and 0.97, respectively. Participants in the highest quantile of OBS had lower odds of abdominal obesity, hypertension, elevated TG, low HDL-C, elevated FBG levels, respectively(WC: OR = 0.61, 95%CI = 0.54–0.69, *P* < 0.0001; hypertension: OR = 0.69, 95%CI = 0.58–0.83, *P* < 0.0001; elevated TG: OR = 0.68, 95%CI = 0.57–0.82, *P* < 0.0001; low HDL-C: OR = 0.60, 95%CI = 0.50–0.70, *P* < 0.0001: elevated FBG: OR = 0.74, 95%CI = 0.62–0.88, *P* < 0.0001). Our results indicated that the removal of any single OBS component did not significantly affect the results for subjects, and the removal of the OBS components brought OR estimates within 5% of the original model results (Table S1). When BMI was removed from OBS, the associations of OBS with the increase of TG and FBG levels were no longer significant, and other OBS components did not alter the associations between OBS

Table 3 Association between OBS and MetS and its components in US adult population

OBS	Q1	Q2	Q3	Q4	P_{trend}	Continuous
Cut-off value	3–15	16–21	22–26	27–37		
High WC						
Model 1	1 (ref)	**0.83(0.75,0.93)**	**0.75(0.66,0.85)**	**0.55(0.49,0.62)**	**< 0.0001**	**0.96(0.96,0.97)**
Model 2	1 (ref)	**0.84(0.75,0.94)**	**0.76(0.66,0.87)**	**0.55(0.49,0.62)**	**< 0.0001**	**0.96(0.95,0.97)**
Model 3	1 (ref)	**0.87(0.77,0.98)**	**0.80(0.70,0.93)**	**0.61(0.54,0.69)**	**< 0.0001**	**0.95(0.94,0.96)**
Elevated TG						
Model 1	1 (ref)	1.00(0.89,1.13)	0.98(0.86,1.11)	**0.82(0.71,0.95)**	**0.008**	**0.99(0.98,1.00)**
Model 2	1 (ref)	0.98(0.86,1.13)	0.96(0.84,1.11)	**0.83(0.72,0.97)**	**0.016**	**0.99(0.98,1.00)**
Model 3	1 (ref)	0.92(0.80,1.06)	**0.85(0.73,0.99)**	**0.68(0.57,0.82)**	**< 0.0001**	**0.98(0.97,0.99)**
Low HDL-C						
Model 1	1 (ref)	**0.75(0.67,0.85)**	**0.73(0.65,0.83)**	**0.55(0.48,0.63)**	**< 0.0001**	**0.97(0.96,0.97)**
Model 2	1 (ref)	**0.79(0.70,0.90)**	**0.78(0.69,0.88)**	**0.60(0.53,0.68)**	**< 0.0001**	**0.97(0.96,0.98)**
Model 3	1 (ref)	**0.79(0.70,0.90)**	**0.78(0.68,0.90)**	**0.60(0.50,0.70)**	**< 0.0001**	**0.97(0.96,0.98)**
Hypertension						
Model 1	1 (ref)	0.97(0.86,1.09)	0.91(0.80,1.03)	**0.73(0.64,0.83)**	**< 0.0001**	**0.98(0.98,0.99)**
Model 2	1 (ref)	0.95(0.82,1.09)	0.93(0.81,1.07)	**0.76(0.65,0.88)**	**< 0.001**	**0.98(0.98,0.99)**
Model 3	1 (ref)	0.92(0.80,1.06)	0.88(0.75,1.03)	**0.69(0.58,0.83)**	**< 0.0001**	**0.98(0.97,0.99)**
Elevated FBG						
Model 1	1 (ref)	0.92(0.81,1.05)	**0.85(0.74,0.97)**	**0.71(0.61,0.82)**	**< 0.0001**	**0.98(0.97,0.99)**
Model 2	1 (ref)	0.92(0.80,1.05)	0.88(0.77,1.00)	**0.78(0.67,0.91)**	**< 0.001**	**0.99(0.98,0.99)**
Model 3	1 (ref)	0.90(0.79,1.04)	**0.85(0.74,0.97)**	**0.74(0.62,0.88)**	0.894	**0.97(0.96,0.98)**
MetS						
Model 1	1 (ref)	**0.85(0.75,0.95)**	**0.77(0.68,0.86)**	**0.60(0.53,0.68)**	**< 0.0001**	**0.97(0.97,0.98)**
Model 2	1 (ref)	**0.84(0.74,0.96)**	**0.78(0.69,0.89)**	**0.63(0.55,0.72)**	**< 0.0001**	**0.97(0.96,0.98)**
Model 3	1 (ref)	**0.81(0.71,0.92)**	**0.72(0.62,0.82)**	**0.55(0.47,0.64)**	**< 0.0001**	**0.96(0.95,0.97)**

Model 1: original model, without adjusting factors; Model 2: adjusted according to age, sex, race, marital status and education level; Model 3: on the basis of Model 2, additionally adjusted energy intake and CRP level. OBS indicates oxidative balance score; MetS, metabolic syndrome; WC, waist circumference; HDL-C, high-density lipoprotein cholesterol; FBG, fasting blood glucose; TG, triglycerides; OR, odds ratio; CI, confidence interval

and MetS and its components ($P_{interaction} > 0.05$). When OBS were categorized into four intervals, the significant associations were no longer observed (Table S2).

Considering that the diagnostic criteria for MetS are slightly different, WC, HDL-C, TG, FBG levels, and blood pressure were used as continuous variables as components of MetS to further analyze the effect of OBS on them (Table S3). We found that higher level of OBS were associated with lower WC (β = -5.99; 95% CI: -6.86,-5.11; $P<0.001$), TG (β = -23.1; 95% CI: -34.6, -11.7; $P<0.001$), SBP (β = -3.25; 95% CI:-4.41, -2.08; $P<0.001$) and DBP (β = -2.33; 95% CI: -3.32, -1.34; $P<0.001$), while it was directly proportional to HDL-C levels in the multivariate model (β=3.75; 95% CI: 2.70, 4.81; $P<0.001$). However, the effect of OBS on FBG levels was not statistically significant ($P=0.228$).

Association between dietary OBS/lifestyle OBS and MetS traits

Figure 1 lists the results of the multivariable logistic regression analysis used to assess the association of dietary and lifestyle OBS with MetS and its components. When dietary OBS/lifestyle OBS was treated as a continuous variable, an increased dietary OBS was negatively related to the risks of MetS (per 1SD, OR=0.89, 95%CI=0.84–0.95) and its components (ORs ranging from 0.86 to 0.90), but not of elevated FBG levels and hypertension (Fig. 1A). For lifestyle OBS, it was significantly and negatively associated with each trait of MetS (Fig. 1A). When dietary OBS and lifestyle OBS were analyzed as categorical variables, the associations of the two OBS with the risk of MetS and its components are shown in Fig. 1B and C, respectively. Dietary OBS showed significant negative associations with MetS (Q4 vs. Q1), HDL-C (Q4 vs. Q1), TG (Q4 vs. Q1), and WC (Q4 vs. Q1) with ORs of 0.75,0.67, 0.74, and 0.72, respectively (Fig. 1B). Lifestyle OBS showed similar significant negative associations with MetS and all its components, with ORs of 0.16, 0.52, 0.43, 0.44, 0.12, and 0.38 for MetS (Q4 vs. Q1), FBG (Q4 vs. Q1), HDL-C (Q4 vs. Q1), TG (Q4 vs. Q1), WC (Q4 vs. Q1), and hypertension (Q4 vs. Q1), respectively (Fig. 1C). This result shows that adherence to antioxidant dietary nutrients has a limited protective effect on MetS, and it is more necessary to adhere to healthy lifestyle behaviors.

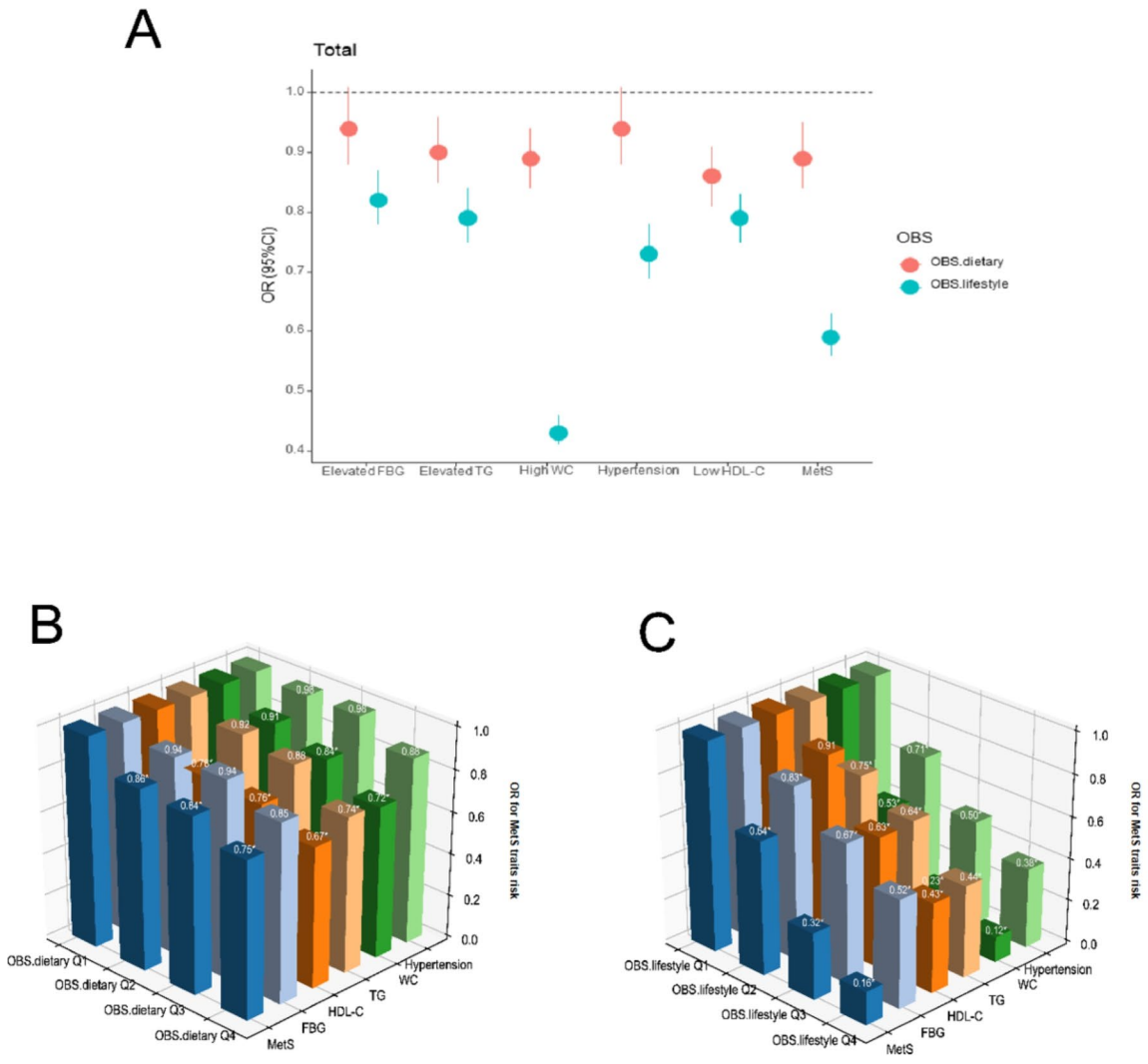

Fig. 1 Association of the dietary/lifestyle OBS as a continuous per SD **(A)** and a categorical variable **(B, C)** with MetS and its components risk. Adjusted for age, sex, race, marital status, education level, energy intake and CRP level. Asterisk refers to significant difference for MetS and its components risk at different dietary/lifestyle OBS interval. OBS indicates oxidative balance score; MetS, metabolic syndrome; WC, waist circumference; HDL-C, high-density lipoprotein cholesterol; FBG, fasting blood glucose; TG, triglycerides; OR, odds ratio; CI, confidence interval

Association of different OBS with MetS traits stratified by sex

The study conducted subgroup analyses and interaction tests, stratified by sex, to assess the consistency of the relationship between OBS and MetS in the general population. Additionally, the aim was to identify potential variations in different population settings. Table S4 shows the relationship between total OBS, dietary OBS and lifestyle OBS and MetS traits discovered by multiple logistic regression in different sex subgroups. In the unadjusted model, there was a significant linear trend for total OBS, dietary OBS and lifestyle OBS and MetS traits in all subgroups (P for trend < 0.0001). After adjusting for all confounding factors, we observed a stable and significant negative association between different OBS and MetS risks in both male and female subgroups. Higher total OBS, dietary OBS, and lifestyle OBS in the highest quartile relative to the lowest quartile, were associated with a notably diminished risk of abdominal obesity, elevated TG and low HDL-C levels. The OBS was negatively associated with the odds of hypertension, while the subgroup analysis by sex unveiled no statistically significant relationship between dietary OBS and hypertension. Intriguingly, an analysis of the association between elevated blood glucose, OBS, and dietary OBS interval odds ratios revealed non-statistically significant results and a lack of dose-response effect among men (Figure S1). In stark contrast, among women, the odds of elevated FBG in the highest OBS interval were statistically significantly

lower 34%, and the OBS-gender interaction was statistically significant ($P_{interaction}$=0.03).

Analysis of restricted cubic spline regression stratified by sex

Subsequently, the relationships between OBS and MetS traits in both men and women were further assessed through the utilization of RCS curves and multivariable logistic regression (model 3, Fig. 2). Figure 2A illustrates a distinct trend of decreasing odds ratio (OR) for MetS with rising OBS, which was consistent across sex subgroups (males: *P* for nonlinear < 0.0001, females: *P* for nonlinear = 0.0054). Interestingly, the OBS was negatively associated with the FBG levels in a linear manner in both males and females. When the study endpoints were WC and TG levels, the non-linearity trend of decreasing OR with increasing OBS was noticed, which remained across sex subgroups. Significant nonlinear relationships were identified between OBS and hypertension (males: *P* for nonlinear < 0.0001, females: *P* for nonlinear = 0.2760) and HDL-C levels (males: *P* for nonlinear < 0.0001, females: *P* for nonlinear = 0.0558) in males and not in female. Despite slight variations observed in the results of the nonlinear analysis of the restricted cubic splines, the overall trends of the MetS traits and OBS remained generally consistent across the plots.

Discussion

In this study, we investigated the association of oxidative homeostasis represented by OBS with MetS and its components in a large US population-based study. Our analysis revealed consistent and negative associations between OBS and MetS, hypertension, dyslipidemia, and abdominal obesity were negative and stable in both males and females. The observed inverse association between OBS and hypertension or FBG levels appeared to primarily influenced by BMI. The association between dietary OBS intervals and elevated FBG levels was not statistically significant in men, whereas the risk was lower by 25% in women. In addition, our findings underscored the significant association of an antioxidant-rich diet and a health-conscious lifestyle on cardiometabolic markers. In essence, the higher the different OBS scores, the lower the risk of MetS and its components. Our findings emphasize the potential benefits of adopting an antioxidant-focused dietary and lifestyle approach for the prevention of MetS and its related health concerns.

The role of vitamins in mitochondrial metabolism and their antioxidant properties suggest that they may play a role in the prevention of MetS. Riboflavin, niacin, vitamin B6, folic acid and vitamin B12 may exert antioxidant effects directly or indirectly through their involvement in mitochondrial respiratory reactions, glycolysis,

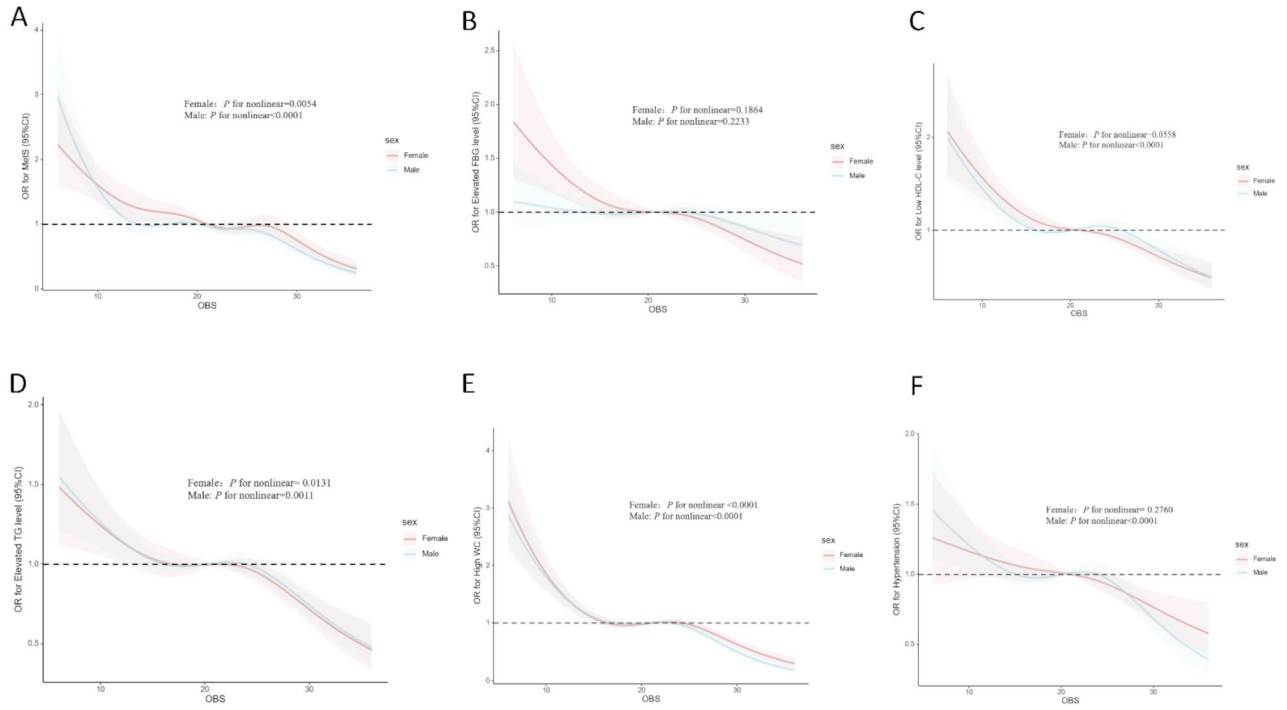

Fig. 2 Dose-response associations between OBS and risk of MetS traits stratified by sex. **(A)** MetS; **(B)** Elevated FBG; **(C)** Low HDL-C; **(D)** Elevated TG; **(E)** High WC; **(F)** Hypertension. The solid lines and shaded areas represent the central risk estimates and 95% CIs. OBS indicates oxidative balance score; MetS, metabolic syndrome; WC, waist circumference; HDL-C, high-density lipoprotein cholesterol; FBG, fasting blood glucose; TG, triglycerides; OR, odds ratio; CI, confidence interval

nucleotide synthesis, or mitochondrial tRNA modification [30]. In addition, adequate micronutrient intake is negatively associated with MetS, which can be partly explained by the inhibition of lipid peroxidation and increased superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR) and glutathione peroxidase (GPX) activities [31].

In 2002, the first OBS scoring system was created, which was based on a combination of the intake of two dietary antioxidants (vitamin C and β-carotene) and a dietary pro-oxidant (iron) [23]. Studies in recent years have taken into account a wider range of factors. For lifestyle factors, studies have shown that physical activity increases antioxidant markers and decreases pro-oxidant markers, regardless of the intensity and type of exercise [32]. Alcohol intake and smoking are the two main factors that play a pro-oxidant role. Chronic alcohol intake induces OS through the oxidation of ethanol to acetaldehyde, which may produce RONS, nucleic acid oxidation, and reduced antioxidant enzyme activity [33]. The OBS of the present study incorporated 16 nutrients and 4 lifestyle factors, enabling a more comprehensive assessment of oxidative stress levels.

To our knowledge, this is the first study to explore whether combined OBS is associated with MetS risk in the US population. We found through literature search that only two studies have evaluated the association between the imbalance of oxidants and antioxidants and MetS, which not only concentrated in the Asian population, but also had heterogeneous results [24, 25]. Our results are consistent with those of the Korean study, which showed a 35% lower risk of MetS in the highest quartile of OBS than Q1 [25]. However, another cross-sectional study recruiting 847 Iranian participants aged 18–65 years found no significant association between OBS and MetS in Tehran adults [24]. The inconsistency between our findings and the Iranian cross-sectional study may be due to different sample sizes and adjustment models in each study as well as different components of the OBS. Due to cultural reasons, the Iranian study did not include enough data about drinking to calculate OBS.

In addition, our study demonstrated that a balance of antioxidant and pro-oxidant exposures reduced the risk of abdominal obesity, dyslipidemia, and hypertension, consistent with previous results from a prospective cohort study in the US [34]. An independent examination from the ATTICA study also revealed a statistically significant reverse correlation between adherence to the Mediterranean diet and serum TG levels [35]. Our study found that when BMI was excluded from OBS, the correlation phase of TG was no longer significant, suggesting that obesity drives this correlation, which is consistent with the general consensus that obesity and insulin resistance are central links in the characteristics of MetS.

In our study, we confirmed that the higher OBS and lifestyle OBS were associated with decreased risk of hyperglycemia. Clinical and animal studies have demonstrated that oxidative stress can disrupt redox reactions in glycolysis, activate alternative glucose metabolic pathways, and ultimately lead to the overproduction of reactive oxygen species (ROS) and lipid peroxidation, thereby triggering a cycle of oxidative stress that exacerbates and worsens hyperglycemia [36–39]. This study pointed out that the phenomenon that oxidative imbalance would affect the increase of FBG was pronounced in women, which might be due to the gender difference in lipid metabolism and the anti-estrogen effect of unhealthy lifestyle that can lead to insulin resistance [40]. Estrogen exerts a powerful antioxidant and antioxidant gene regulatory role by stimulating the expression and activity of antioxidant enzymes, such as superoxide dismutase and glutathione peroxidase [41]. In contrast, androgens are thought to induce OS because they increase metabolic rate, which may increase ROS production by increasing oxygen consumption [42]. In addition, in one study, men consumed higher levels of processed meats and sugary beverages than women, which can lead to inflammation, insulin resistance, and OS. High intake of these specific foods may strongly attenuate the beneficial properties of high dietary OBS on fasting glucose reduction in men. The present investigation examined the correlation between each component and elevated FBG levels, revealing that the prooxidative factor BMI contributed to the elucidation of the interaction between OBS and gender. Nevertheless, further exploratory basic science or clinical inquiries are warranted to comprehensively understand potential gender-based distinctions in the mechanism by which oxidative stress contributes to the elevation of FBG levels.

This study possesses several notable advantages. First of all, compared with other studies, this study comprehensively considered the oxidative potential of dietary nutrients and lifestyle behaviors on the occurrence and development of MetS. Secondly, our utilization of a complex multi-stage probability sampling design ensures the selection sample from the civilian non-institutionalized resident population. This enables us to extend findings of our findings to encompass all civilian non-institutionalized adult residents within the United States. Thirdly, our study adjusted for various confounding factors. Fourthly, the sensitivity analysis results exhibited that the key conclusions of this study were robust. Furthermore, OBS can be used as a predictive tool to comprehensively assess the degree of association between the overall state of oxidative balance and MetS. Consequently, the implications of our findings extend into the realm of public

health, holding promise for bolstering MetS prevention strategies.

Simultaneously, our study does harbor certain potential limitations that warrant acknowledgment. We used self-reported intakes to assess pro- and anti-oxidant exposures. Although using 24-hour dietary reviews, there is an inevitable recall bias. The dietary questionnaires may only capture some possible nutrient sources and consider their bioavailability. In addition, OBS calculations omitted the consideration of endogenous factors impacting cellular antioxidant defense, DNA damage and repair, cell growth, and cell death attributed to the availability of database variables. Thirdly, since the study was a cross-sectional study, it was difficult to elucidate a causal relationship between OBS and MetS. Reverse causal associations cannot be ruled out for the time being. Therefore, more prospectively designed studies are needed to demonstrate the effectiveness of OBS and we will continue to validate the predictive ability of OBS using cohort studies in the future.

In conclusion, by estimating the possibility of OBS as a predictor of MetS risk, it is found that higher OBS (indicating dominant antioxidant exposure) is associated with lower MetS and its components risk, which is not affected by a specific component of OBS construction. The association of dietary OBS with FBG was gender-specific. The results of this study showed that the imbalance of oxidation suggests the existence of metabolic disorders. The negative association of OBS with FBG and TG levels were mainly driven by obesity. Comparatively, amalgamating diverse pro- and anti-oxidative exposures into a unified score proves to be a more effective approach in evaluating oxidative stress-related factors encompassing obesity, dietary nutritional attributes, and lifestyle behaviors. Embracing an antioxidant-rich diet and lifestyle emerges as a preventive strategy against the onset of metabolic disorders.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13098-024-01500-y.

Supplementary Material 1

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Author contributions

J.L. : Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. Y. L. , J.L. : Writing – review & editing, Validation, Resources, Investigation. Z.F. , L.B., Y.F., P.Z. and F.S. : Writing – review & editing, Validation, Supervision, Resources, Conceptualization.

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Data availability

The data underlying this article are available in NHANES, at https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with Declaration of Helsinki and was approved by the Ethics Committee of Tianjin Medical University Cancer Hospital.

Competing interest

The authors declare that they have no competing interests.

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