Research Article

Association of Oxidative Balance Score with the Metabolic Syndrome in a Sample of Iranian Adults

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Objective. We aimed to assess the association of the oxidative balance score (OBS) with metabolic syndrome (MetS) in adults.

Design. A population-based cross-sectional study

Setting. Health centers from five districts in Tehran, Iran.

Methods. We recruited 847 participants with an age range of 18-65 years. Dietary intake was assessed by a semiquantitative food frequency questionnaire with 168 items. The OBS was calculated by using the following 13 dietary and nondietary anti- and prooxidant components: dietary antioxidants (selenium, fiber, β-carotene, vitamin D, vitamin C, vitamin E, and folate), dietary prooxidants (iron and saturated and polyunsaturated fatty acids), and nondietary anti- (physical activity) and prooxidants (smoking and obesity). The odds ratio (OR) and 95% confidence interval (CI) of the MetS and its components across tertiles of the OBS were calculated by logistic regression analysis, controlling for age, sex, energy intake, occupation, and educational level.

Results. The range of OBS was between 16 and 39. Being in the top versus the bottom tertile of the OBS was not associated with the MetS (OR = 0.71, 95% CI 0.48-1.03; P = 0.07), after controlling for potential confounders. Higher OBS score was associated with a lower likelihood of abdominal obesity (OR: 0.55, 95% CI: 0.38-0.81; P = 0.003) and increased diastolic blood pressure (OR: 0.64, 95% CI: 0.41-0.99; P = 0.04). Higher OBS was not associated with other components of the MetS. Conclusion. Overall, the present study showed that there was no significant relationship between OBS and MetS in Tehranian adults.

1. Introduction

The metabolic syndrome (MetS) is a collection of several metabolic disorders including abdominal obesity, dyslipidemia, hypertension, hyperglycemia, inflammation, high body mass index (BMI), and insulin resistance [1]. The incidence of MetS often occurs in parallel with the incidence of obesity and type 2 diabetes [2]. The prevalence of MetS is about 20-30% of the adult’s population in developed countries [3]. The occurrence of MetS and obesity is increasing in Iran [4, 5]. Around one-third of adults in Iran are affected by MetS [6].

MetS is a consequence of a complex interaction between several factors such as unhealthy dietary patterns and lifestyle-related factors [2, 7]. It has been proposed that oxidative stress may be involved in the pathogenesis and progression of MetS [8]. Obesity seems to exacerbate the body’s oxidant/antioxidant balance in favour of free radicals and oxidative stress [9–11]. As body weight increases, the ability of the antioxidant defence system decreases to stop the activities of free radicals, so multifactorial metabolic disorders such as hypertension will appear [12]. Free radicals can damage DNA, proteins, and lipids, leading to cell injury and unfavourable health outcomes like tissue injury that is related to vascular damage [13]. There is evidence that higher dietary antioxidant intake can mitigate levels of oxidative stress and metabolic disorders, namely, diabetes and
inflammation [14, 15]. Researchers have presented that a 
combination of antioxidant components can be more 
strongly associated with metabolic disorders than any indi-
vidual antioxidant nutrient [16]. In addition to anti- and pro-
antioxidant dietary components, other lifestyle-related 
behaviours such as cigarette smoking [17], physical activity 
[18], and adiposity [19] can affect levels of oxidative stress 
in the body. So to capture the whole oxidant/antioxidant 
properties of lifestyle, Goodman et al. introduced an oxida-
tive balance score (OBS) as a measure of combined pro-
and antioxidant exposure status of an individual, with a 
higher score indicating a predominance of anti- over proox-
idant exposures [20, 21]. Several studies have investigated the 
association between OBS and various chronic diseases like 
different cancer types and cardiovascular diseases and 
inflammation [13, 22–24].

Considering the role of oxidative stress in the develop-
ment of MetS [25], this study was aimed at examining the 
association of the OBS, a proxy of combined anti- and proox-
idant properties of the diet and lifestyle, with the risk of MetS 
in a sample of Tehranian adults, hypothesizing that a higher 
OBS would be associated with a lower risk of MetS.

2. Methods

2.1. Study Participants. The sample size required for this 
study was calculated by considering the frequency of obesity 
as a dependent variable using the following formula. Taking 
into account the total prevalence of overweight and obesity of 68.5% in 
Tehran adults, with 95% confidence and a maximum estimation error of 5% and a value of 0.04 as the effect size, the sample size was 546.

\[
n = \frac{z^2 \cdot p(1-p)}{d^2} = \frac{(1/65)^2 \times 0.65 \times 0.35}{(0.04)^2} = 546.
\]  

(1)

Due to the fact that cluster sampling is two-stage and the 
response of individuals in each health center may be corre-
lated, the number of samples is multiplied by the effect factor 
of the cluster design selected as 1.5, and the total number of 
samples 819 is obtained, which we consider as 850, because this data is taken from the previous design and the effect of dietary pattern on obesity is more sensitive than its effect on cardiometabolic and inflammatory biomarkers; in the present study, the sample size of 850 is considered.

Eight hundred fifty adult males and females referred to the 
health care centers in different zones of Tehran took part in 
the present cross-sectional study. Five zones including North, 
South, West, East, and the center of the city were selected. 
Next, a list of all health care centers that existed in each zone 
was provided. We randomly chose eight health centers from 
five districts (40 health centers) and then divided the total 
sample size (850) by the number of health centers (40) to 
obtain the number of participants in each health center. Inclu-
sion criteria were apparently healthy male and female, aged 
between 20 and 59 years, living in Tehran city, who attended 
the local health care centers during the study period (2018- 
2019), and had a willingness to take part in the study.

2.2. Ethical Approval. All participants gave written informed 
consent before their inclusion in the study. The study was 
performed in accordance with the Declaration of Helsinki, 
and the procedure of the study was approved by the Research 
Ethics Committee of Tehran University of Medical Science 
(Ethic Number: IR.TUMS.VCR.REC.1397.157). Detailed 
written information regarding the background and proce-
dures of the study was presented to participants.

2.3. Demographic Factors. At the first visit at each health cen-
ter, data about gender (male, female), age, education (under 
diploma, diploma), smoking status (current smoking, former 
smoking, never smoking), occupation (employed, retired, 
housekeeper, or unemployed), and marital status (married or 
other) were collected by trained interviews through pre-
specified data extraction forms.

2.4. Physical Activity. The validated International Physical 
Activity Questionnaire (IPAQ) was utilized for determining 
physical activity levels [26]. Metabolic equivalent (MET) 
was used for calculating the level of physical activity [27]. 
Participants were categorized into two groups including very 
low (<600 MET-minute/week) or low (600–3000 MET-min-
ute/week) and moderate and high physical activity (>3000 
MET-minute/week).

2.5. Anthropometric and Blood Pressure Assessments and 
Laboratory Tests. A wall stadiometer with a sensitivity of 
0.1 cm (Seca, Germany) was used for measuring the partici-
pants’ height. They were asked to take off their shoes for 
height measurement. Participants’ weight was measured, 
without coat and jacket, by using an adult’s digital scale 
(808Seca, Germany) with 0.1 kg precision. BMI was calcu-
lated as weight in kilograms divided by height in meters 
squared. Waist circumference (WC) was measured with a 
tape measure to the nearest 0.1 cm between the iliac crest 
and the lowest rib during exhalation. After 10 to 15 minutes 
of rest and sitting, systolic (SBP) and diastolic (DBP) blood 
pressure was measured by a trained physician, on the right 
arm, with a digital barometer (BC 08, Beurer, Germany). 
For each participant, the mean of two blood pressure mea-
surements was recorded. Fasting plasma glucose (FPG), 
serum triglyceride (TG), and high-density lipoprotein cho-
lesterol (HDL-C) were measured after 10–12 hours of over-
night fasting from a venous blood sample. Blood samples 
were measured by standard methods at the Nutrition and 
Biochemistry Laboratory of the School of Nutritional Sci-
ences and Dietetics at Tehran University of Medical Sciences.

2.6. Dietary Assessment. A semiquantitative food frequency 
questionnaire with 168 items [28] was used for assessing 
the average dietary intake during the past year. The fre-
quency eating (daily, weekly, monthly, and annual) of each 
food in the food frequency questionnaire was recorded in 
an interview by trained dieticians. Collected data were con-
verted into g/d according to household measures by using 
Nutritionist IV software based on the Iranian food-
modified US Department of Agriculture food composition database [29].
2.7. Definition of Metabolic Syndrome. The diagnostic criteria introduced by NCEP ATP III [30] was used to define cardio-metabolic abnormalities, and accordingly, the metabolic syndrome was established when three or more of the following disorders were presented: (1) central obesity as WC $\geq 102$ cm in men and $\geq 88$ cm in women; (2) hypertriglyceridemia as serum TG $\geq 150$ mg/dL (1.69 mmol/L); (3) HDL-C $< 40$ mg/dL (1.04 mmol/L) for men and $< 50$ mg/dL (1.29 mmol/L) for women; (4) hypertension as systolic/diastolic blood pressure $\geq 130/85$ mmHg or taking antihypertensive medications; and (5) hyperglycemia as FPG $\geq 100$ mg/dL (5.6 mmol/L) or taking antidiabetic medications.

2.8. Oxidative Balance Score. We used the method introduced by Goodman et al., to calculate the OBS of each participant. According to this method, a total of 13 dietary and nondietary pro- and antioxidant components, based on a priori knowledge about their association to oxidative stress, were

| Characteristics | T1 [16–24] (n = 278) | T2 [25–28] (n = 311) | T3 [29–39] (n = 258) | P value* * |
|----------------|-----------------------|-----------------------|-----------------------|------------|
| Gender (%)     |                       |                       |                       |            |
| Male           | 38.3%                 | 33.8%                 | 27.8%                 | 0.68       |
| Female         | 30.3%                 | 38%                   | 31.7%                 |            |
| Education (%)  |                       |                       |                       |            |
| Illiterate     | 27.8%                 | 37.5%                 | 34.7%                 |            |
| Under diploma  | 35%                   | 33.6%                 | 31.4%                 | 0.18       |
| Diploma        | 31.5%                 | 33.8%                 | 34.6%                 |            |
| Educated       | 33.6%                 | 41.4%                 | 25%                   |            |
| Smoking (%)    |                       |                       |                       |            |
| Current        | 50%                   | 22.7%                 | 27.3%                 | 0.007      |
| Former         | 50%                   | 17.6%                 | 32.4%                 |            |
| Never          | 31.1%                 | 38.4%                 | 30.6%                 |            |
| Physical activity (MET-min/day) | | | | |
| Low            | 37.4%                 | 35.4%                 | 27.2%                 | <0.001     |
| Medium or high | 24.8%                 | 39%                   | 36.1%                 |            |

Abbreviations: BMI: body mass index; MET: metabolic equivalent; OBS: oxidative balance score; PUFA: polyunsaturated fatty acid; SFA: saturated fatty acid; T: tertile; WC: waist circumference. * Data are presented as a percentage for categorical variables and mean ± standard deviation for continuous variables. **The one-way analysis of variance and the chi-square test, respectively, were used for comparison of continuous and categorical variables among tertiles of the OBS. P < 0.05 is statistically significant. aBecause the number of people with high physical activity was low, we combined them with moderate physical activity.
BMI < 30 kg/m² in males and ≥ 30 kg/m² in females, and ≥ 88 cm in males or ≥ 88 cm in females, and > 3: never smoking. The score of four components was then summed to calculate the OBS for each participant.

The initial sample size included 850 participants; of those, three participants were excluded due to lack of data for at least one variable. Therefore, 847 participants were included in the present study. Characteristics of the participants and dietary intake across tertiles of the OBS are indicated in Table 1. The mean age of participants was 44.7 ± 10.7 years, of whom 31.3% were men. The prevalence of MetS was 30.5%. The range of the OBS was between 16 and 36. Compared to those in the lowest tertile of the OBS, participants in the highest tertile were more likely to have lower BMI and WC and lower iron intake. Besides, those with a higher level of OBS had a higher intake of vitamins C, D, and E, fiber, beta-carotene, and folate. There were no significant differences in gender, age, smoking status, and dietary intake of selenium, PUFA, and SFA across tertiles of the OBS.

Table 2 indicates the biochemical variables of the participants across tertiles of the OBS. There were no significant differences in terms of biochemical variables across tertiles of the OBS. Table 3 represents the OR and its 95% CI of MetS and its components across tertiles of the OBS. The results showed that there was no significant association between OBS and MetS. The OR of MetS for the third versus first tertile of the OBS was 0.71 (95% CI: 0.48, 1.03; P = 0.07) in the fully adjusted model. There were significant relationships between higher levels of OBS and abdominal obesity as assessed by WC (OR = 0.55, 95% CI: 0.38, 0.82; P = 0.003) and increased DBP (OR: 0.64, 95% CI: 0.41, 0.99; P = 0.04). There was no significant association between the OBS and other components of the MetS.

4. Discussion

Oxidative stress is associated with several health outcomes like diabetes, inflammation, different types of cancer, and other metabolic disorders [13, 15, 22]. To the best of our knowledge, no previous study has been done to investigate the relationship between this score and MetS in Iran. In this cross-sectional study of Tehranian adults, we assessed the status of oxidative balance, represented by OBS, and its association with MetS. There was no significant association between OBS and MetS either in crude or in the fully adjusted models. There was also no significant relationship between OBS and components of the MetS, except for increased WC and DBP.

Current evidence regarding the association of a priori OBS and the risk of chronic diseases is inconsistent. Two prospective cohort studies showed that a balanced oxidative status was associated with a lower risk of all-cause and cause-specific mortality [24, 31]. Some case-control studies suggested an inverse association between the OBS and the likelihood of colorectal and prostate cancers [20, 21, 32]. One large cohort study found an inverse association between the OBS and colorectal cancer risk [33], whilst two other case-cohort studies suggested no association between the OBS and prostate cancer risk [34, 35].
Table 3: The association between oxidative balance score and metabolic syndrome in Tehranian adults (odds ratio and 95% confidence interval).

| Oxidative balance score | T1        | T2        | T3        |
|-------------------------|-----------|-----------|-----------|
| Cut points of tertiles  | 16-24     | 25-28     | 29-39     |
| Participants (n)        | 278       | 311       | 258       |
| High WC                 |           |           |           |
| Crude                   | 1.0       | 0.98 (0.71-1.35) | 0.77 (0.55-1.08) |
| P value*                | 0.89      |           | 0.13      |
| Model I                 | 1.0       | 0.82 (0.57-1.18) | 0.56 (0.38-0.82) |
| P value                 | 0.286     |           | 0.003     |
| Model II                | 1.0       | 0.85 (0.59-1.22) | 0.55 (0.38-0.81) |
| P value                 | 0.37      |           | 0.003     |
| High FPG                |           |           |           |
| Crude                   | 1.0       | 1.21 (0.84-1.75) | 0.73 (0.48-1.10) |
| P value                 | 0.30      |           | 0.13      |
| Model I                 | 1.0       | 1.21 (0.83-1.74) | 0.73 (0.48-1.10) |
| P value                 | 0.32      |           | 0.13      |
| Model II                | 1.0       | 1.20 (0.83-1.74) | 0.72 (0.48-1.10) |
| P value                 | 0.33      |           | 0.13      |
| High serum TG           |           |           |           |
| Crude                   | 1.0       | 1.07 (0.77-1.49) | 0.80 (0.56-1.14) |
| P value                 | 0.680     |           | 0.22      |
| Model I                 | 1.0       | 1.06 (0.76-1.48) | 0.80 (0.56-1.14) |
| P value                 | 0.72      |           | 0.21      |
| Model II                | 1.0       | 1.07 (0.77-1.50) | 0.78 (0.56-1.14) |
| P value                 | 0.67      |           | 0.21      |
| High serum total cholesterol |       |           |           |
| Crude                   | 1.0       | 1.17 (0.84-1.62) | 1.19 (0.84-1.68) |
| P value                 | 0.351     |           | 0.32      |
| Model I                 | 1.0       | 1.15 (0.83-1.60) | 1.17 (0.83-1.65) |
| P value                 | 0.41      |           | 0.38      |
| Model II                | 1.0       | 1.12 (0.80-1.56) | 1.17 (0.83-1.66) |
| P value                 | 0.50      |           | 0.37      |
| Low serum HDL-C         |           |           |           |
| Crude                   | 1.0       | 0.88 (0.62-1.26) | 0.87 (0.60-1.25) |
| P value                 | 0.49      |           | 0.44      |
| Model I                 | 1.0       | 1.08 (0.72-1.60) | 1.06 (0.70-1.61) |
| P value                 | 0.712     |           | 0.778     |
| Model II                | 1.0       | 1.07 (0.72-1.60) | 1.07 (0.70-1.62) |
| P value                 | 0.73      |           | 0.76      |
| High systolic blood pressure |     |           |           |
| Crude                   | 1.0       | 1.22 (0.85-1.74) | 1.09 (0.74-1.59) |
| P value                 | 0.28      |           | 0.66      |
| Model I                 | 1.0       | 1.18 (0.79-1.78) | 0.90 (0.58-1.38) |
| P value                 | 0.41      |           | 0.63      |
| Model II                | 1.0       | 1.20 (0.80-1.82) | 0.91 (0.59-1.40) |
| P value                 | 0.38      |           | 0.66      |
Evidence regarding the association of the OBS and the MetS is scarce. Our preliminary search found only one study that assessed the association of oxidant/antioxidant disequilibrium and MetS [36]. A recent cross-sectional study among 6400 Korean adults aged >40 years showed that those in the fourth quartile of the OBS had 35% lower odds of the MetS as compared to those in the first tertile. They included dietary anti- (vitamin C, carotene, and retinol) and prooxidants (iron) and nondietary components including smoking status, physical activity, and alcohol drinking to calculate the OBS [36]. The inconsistency between our findings and the Korean cross-sectional study may be due to different sample sizes and adjustment models and different components of the OBS in each study. Due to cultural reasons, we did not have sufficient data regarding alcohol drinking to include in the OBS. Also, different dietary components were used to calculate the OBS in two studies.

Another cross-sectional study in Thailand showed that those with the MetS had lower circulating levels of superoxide dismutase, catalase, and vitamin C than those without the MetS [37]. However, they used serum biomarkers to evaluate oxidant/antioxidant disequilibrium.

We also found no association between the OBS and most components of the MetS. Exceptions were increased DBP and WC, for which inverse associations were found. Our results regarding the null association between the OBS and high fasting glucose and SBP and inverse associations with increased DBP and WC are consistent with those of the Korean cross-sectional study [36]. However, in contrast to their findings, we found no association between OBS and the likelihood of hypertriglyceridemia and low HDL-C concentration.

Another cross-sectional evaluation within a prospective cohort study in the US found inverse associations between the OBS and increased WC and low-density lipoprotein cholesterol concentration, and no association for total cholesterol and TG [38]. The dietary components used to calculate the OBS in that study were the intake of vitamin C, α-carotene, β-carotene, β-cryptoxanthin, lutein, lycopene, selenium, iron, and PUFA, as well as nondietary factors including smoking history, alcohol drinking, and the use of aspirin and other nonsteroid anti-inflammatory drugs.

Although we did not find a significant relation between OBS and the MetS, several biological pathways suggest a link between oxidative stress and cardiometabolic disorders [13]. Recent studies suggest that a high level of oxidative stress may increase the risk of MetS by activating proinflammatory mediators [39] and several transcriptional, molecular, and metabolic pathways. Oxidative stress is an underlying pathologic mechanism of insulin resistance [40, 41] and thereby can exert unfavourable impacts in the pathways of glucose metabolism, blood pressure, and serum lipid abnormalities [42]. Oxidative stress is accompanied by the more production of reactive oxygen species. The reactive oxygen species can induce lipid peroxidation, which in turn is associated with several cardiometabolic abnormalities [43]. In addition to the toxic effects of the reactive oxygen species, they can decrease the endothelial production of nitric oxide [12]. Studies found that levels of nitric oxide in obese patients who have hypertension were lower than those without hypertension [12, 44].

One of the strengths of our study was the ability to include both dietary and lifestyle components into the score, so a comprehensive view of different determinants of oxidative stress was provided. Our study included a relatively large sample size involving both men and women. In addition, data was collected by expert dieticians with valid and reliable questionnaires. On the other hand, our study has some limitations which can affect the results. Because of cross-sectional design and the temporal sequence, as a result, a casual association cannot be concluded. Moreover, some items were missing in the OBS (i.e., alcohol drinking). Also, the known

### Table 3: Continued.

| Oxidative balance score | T1      | T2                      | T3                      |
|-------------------------|---------|-------------------------|-------------------------|
| **High diastolic blood pressure** |         |                         |                         |
| Crude                   | 1.0     | 1.04 (0.71-1.51)         | 0.72 (0.47-1.09)         |
| P value                 | 0.85    | 0.64 (0.41-0.98)         | 0.04                    |
| Model I                 | 1.0     | 1.02 (0.68-1.51)         | 0.64 (0.41-0.99)         |
| P value                 | 0.96    | 0.64 (0.41-0.99)         | 0.04                    |
| Model II                | 1.0     | 0.94                    |                         |
| P value                 |         | 0.72 (0.47-1.09)         |                         |
| **MetS**                |         |                         |                         |
| Crude                   | 1.0     | 0.96 (0.68-1.36)         | 0.71 (0.49-1.04)         |
| P value                 | 0.83    |                         | 0.08                    |
| Model I                 | 1.0     | 0.95 (0.67-1.35)         | 0.71 (0.48-1.03)         |
| P value                 | 0.79    | 0.71 (0.48-1.03)         |                         |
| Model II                | 1.0     | 0.96 (0.67-1.36)         | 0.71 (0.48-1.03)         |
| P value                 | 0.82    | 0.71 (0.48-1.03)         | 0.07                    |

Abbreviations: FPG: fasting plasma glucose; HDL: high-density lipoprotein; LDL: low-density lipoprotein; MetS: metabolic syndrome; TG: triacylglycerol; WC: waist circumference. *P values from Mantel-Haenszel extension test. Model I: adjusted for age, sex, and energy intake; Model II: additionally adjusted for occupation and educational level.
limitations of FFQ for dietary assessment, i.e., the error in recall and limited food choices, should be considered. Finally, we had a lack of information about genotypes that can affect OBS and components of the MetS [38]. We also did not include endogenous factors which may affect oxidative stress [15].

5. Conclusions

In conclusion, no significant association between OBS and odds of MetS in adults was found. However, a significant inverse association was found between OBS and abdominal adiposity and DBP. Further studies, in particular those with inverse association was found between OBS and abdominal adiposity and DBP. Further studies, in particular those with prospective nature, need to confirm the present findings.

Abbreviations

BMI: Body mass index
MET: Metabolic equivalent
OBS: Oxidative balance score
PUFA: Polyunsaturated fatty acid
SFA: Saturated fatty acid
WC: Waist circumference
HDL-C: High-density lipoprotein cholesterol
FPG: Fasting plasma glucose
LDL: Low-density lipoprotein
MetS: Metabolic syndrome
TG: Triacylglycerol.

Data Availability

The data support the findings of this study and are available from the corresponding author upon reasonable request.

Ethical Approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving research study participants were approved by the ethics committee of the Tehran University of Medical Sciences.

Consent

Written informed consent was obtained from all subjects/patients.

Disclosure

The funder had no role in the design, analysis, or writing of this article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

SSb and KDj contributed to the conception/design of the research; EA and FDF contributed to the acquisition of data; ZN and MF participated in the analysis and interpretation of the data; ZN drafted the manuscript; AJ critically revised the manuscript; and SS-b agrees to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

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