



OPEN The association between dietary intakes of nitrate and nitrite and odds of metabolic syndrome and its component in adults

Atieh Mirzababaei^{1,2}✉, Maryam Mahmoodi³, Abbasali Keshtkar⁴, Haleh Ashraf⁵, Fereshteh Pashayee-Khamene⁶, Pardis Khalili⁷ & Khadijeh Mirzaei¹✉

Metabolic syndrome (MetS), a cluster of conditions including central obesity, elevated blood pressure, high fasting blood glucose, high triglycerides, and low high-density lipoprotein cholesterol (HDL-C) cholesterol, has increased in prevalence worldwide. The evidence on the association between intakes of nitrate (NO_3^-) and nitrite (NO_2^-) and MetS is scarce and inconsistent. This study examined the association between dietary intakes of NO_3^- and NO_2^- with MetS in Iranian adults. This cross-sectional study was conducted on the baseline phase of the Tehran University of Medical Sciences Employee's Cohort study (TEC). A total of 4027 adults aged 20 years or over were included (mean age: 40.72 ± 8.68 years). Dietary intakes of NO_3^- and NO_2^- were estimated using a validated dish-based food frequency questionnaire (FFQ) with 144 items. MetS was defined according to the diagnostic criteria proposed by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP). Data were analyzed using independent t-tests, chi-square tests, ANOVA, ANCOVA, and logistic regression models adjusted for potential confounders. A P-value < 0.05 was considered statistically significant. While there was no significant association between the highest intake of NO_3^- and MetS, participants in the third quintile of NO_3^- were less likely to have MetS. However, no significant association between NO_2^- and MetS intake was observed. Adults with the highest intake of NO_3^- were 26%, 30%, and 25% lower odds of having hypertension (HTN), low HDL-C, and abdominal obesity compared to the lowest intake. Furthermore, participants with the highest intake of NO_2^- compared to the lowest intake were 56%, 21%, and 22% lower odds of having hypertension, abdominal obesity, and low HDL-C, respectively ($P < 0.05$). While a negative association between NO_2^- and NO_3^- intake from plant sources and HTN and low HDL-C, a positive association between NO_2^- and NO_3^- intake from animal sources and HTN and hyperglycemia. Our findings showed that higher intakes of nitrate and nitrite were associated with lower odds of several MetS components. Further prospective studies are needed to provide evidence to compare with our findings.

Keywords Nitrate, Nitrite, Metabolic syndrome, Iranian adults, Hypertension, Abdominal obesity

Abbreviations

ALK	Alkaline phosphatase
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ANCOVA	Analysis of covariance
BMI	Body mass index

¹Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, P.O. Box:14155-6117, Tehran, Iran. ²Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. ³Department of Cellular and Molecular Nutrition, School of Nutritional Science and Dietetics, Tehran University of Medical Sciences, Tehran, Iran. ⁴Department of Disaster and Emergency Health, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. ⁵Cardiac Primary Prevention Research Center, Cardiovascular Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran. ⁶Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. ⁷Department of Nutrition, Science and Research Branch, Islamic Azad University, Tehran, Iran. ✉email: ati_babaei@yahoo.com; mirzaei_kh@sina.tums.ac.ir

BIA	Bioelectrical impedance analyzer
CVD	Cardiovascular diseases
DBP	Diastolic blood pressure
eNOS	Cell-derived nitric oxide synthase
FBS	Fasting blood sugar
FFQ	Food frequency questionnaire
HC	Hip circumference
HTN	Hypertension
HDL_C	High-density lipoprotein cholesterol
LDL_C	Low-density lipoprotein cholesterol
IPAQ	International physical activity questionnaire
MetS	Metabolic syndrome
NAFLD	Non-alcoholic fatty liver disease
NO	Nitric oxide
NO ₂ ⁻	Nitrite
NO ₃ ⁻	Nitrate
NOS	Nitric oxide synthase
NCEP ATP III	National cholesterol education program adult treatment panel III
PA	Physical activity
SBP	Systolic blood pressure
SES	Social economic status
SD	Standard deviation
TC	Total cholesterol
TG	Triglycerides
WC	Waist circumference
WHR	Waist-hip ratio

Metabolic syndrome (MetS) is a chronic non-infectious condition characterized by central obesity, low HDL-C cholesterol, high blood pressure, elevated fasting blood glucose, and high triglyceride levels^{1,2}. MetS increases the risk of metabolic diseases such as type 2 diabetes and cardiovascular disease (CVD)³. Evidence indicates that adopting a healthy lifestyle, engaging in regular physical activity, and consuming functional foods and a balanced diet can help prevent or manage MetS⁴⁻⁶. Obesity and related non-communicable diseases have increased in both high-income and low-middle-income countries⁷⁻⁹ which elevates the risk of MetS. The Eastern Mediterranean Region (EMR), including the Middle East and North African countries, has been reported to have the highest MetS prevalence¹⁰. Iran is the second most highly populated country in the Middle East, with around 23% of the Iranian population over 20 years old having MetS in 2018¹¹. It has been found that improving diet quality has a positive impact on MetS¹². Furthermore, the existing evidence showed that dysfunctions in different nitric oxide (NO) pathways contribute to the pathogenesis of MetS¹³. Dietary nitrate (NO₃⁻) intake has been shown to be inversely associated with several atherogenic indices¹⁴. Dietary nitrate (NO₃⁻) is an important source of Nitric oxide (NO) and other nitrogen oxides (Fig. 1).

Plant foods, particularly leafy vegetables such as arugula and spinach, contain the highest levels of nitrates. In most populations, fruits and vegetables contribute about 80% of total dietary nitrate intake, whereas drinking water accounts for less than 14%^{13,15}. The L-arginine converts to citrulline in the body, synthesizing the main NO through cell-derived nitric oxide synthase (eNOS). The cyclic guanosine monophosphate (cGMP) is produced through NO diffusion to the smooth muscle cells, resulting in vascular wall relaxation¹⁶. Recent evidence indicates that vegetables rich in NO₃⁻, such as beets, can reduce both systolic and diastolic blood pressure (BP), protect endothelial function, prevent re-ischemia, and suppress cell proliferation, thereby reducing angiogenesis, inflammation, and promoting apoptosis^{17,18}.

Recent studies have reported that diets with a high dose of NO₃⁻ can improve endothelial conditions, thus, continuous NO production is necessary to avoid cardiovascular system damage^{19,20}. On the other hand, diet may indirectly affect cardiovascular diseases, by eating meaty foods, the levels of gut microbiome components such as trimethylamine N-oxide and kynurenine are increased, which are then implicated in the development of several chronic inflammations and metabolic diseases²¹. Furthermore, changes in bioactivity and bioavailability or dysregulation in the metabolic pathway of NO have an important effect on vascular function, inflammation, BP, and the pathogenesis of many risk factors associated with type 2 diabetes, CVD, and MetS^{19,22}.

However, the existing evidence on the association between NO₃⁻ and NO₂⁻ dietary intake and MetS is mixed. While Carlström et al. 2010 showed that 10 weeks of dietary NO₃⁻ can produce NO in the NO₃⁻-nitrite (NO₂⁻)-NO pathway in eNOS knock-out mice with high BP, TG, sugar blood, and obesity²³, Matthews et al. 2018 found that dietary NO₃⁻ did not have any effect on preventing the progression of MetS in mice fed with a high-fat diet²⁴. An animal study reported that long-term dietary NO₃⁻/NO₂⁻ deficiency contributed to CVD, vascular complications, and MetS. Furthermore, Ohtake et al. 2022 indicated that NO deficiency might underlie postmenopausal MetS, and dietary NO₃⁻/NO₂⁻ may compensate for this deficiency by producing endogenous NO²⁵. Dietary nitrate can be converted into cancer-related metabolites such as nitrosamines. However, providing NO₂⁻ and NO₃⁻ from fruits and vegetables could be non-carcinogenic due to the compounds such as polyphenols that inhibit the synthesis of nitrosamines in the stomach^{26,27}.

Recent reviews have also highlighted the role of phytochemicals and plant-based dietary patterns in improving MetS-related parameters^{28,29}.

While several human and animal studies reported positive effects of NO₃⁻ and NO₂⁻ intake on MetS^{30,31} no study has investigated the dietary intake of NO₃⁻ and NO₂⁻ in relation to MetS in Iranian adults. Previously,

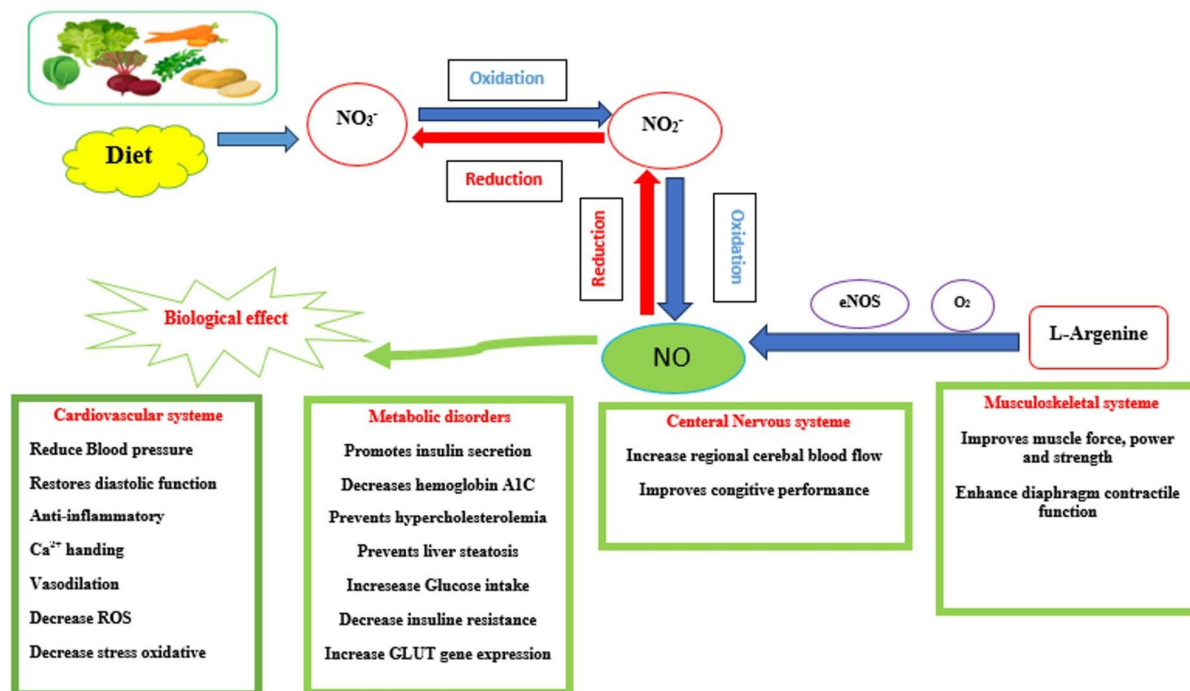


Fig. 1. A schematic diagram of the nitrite and nitric oxide (NO) from exogenous (dietary) and endogenous sources and biological effects of NO.

we showed the significant interaction between NO_3^- and NO_2^- and gut microbial metabolites including trimethylamine N-oxide (TMAO) and kynurenine (KYN) on MetS³². As a result, this study for the first time, assessed the association between the total intake of NO_3^- and NO_2^- and MetS. Furthermore, the link between dietary intake of NO_3^- and NO_2^- from, animal and plant sources and MetS was investigated in Iranian adults. In addition to dietary nitrate and nitrite, other bioactive compounds such as Coenzyme Q10 have been reported to improve certain MetS parameters, including triglyceride and HDL-C levels³³. Considering such compounds helps to provide a broader nutritional context for MetS management.

Materials and methods

Study design and population

This cross-sectional study used the data from the baseline phase of the Tehran University of Medical Sciences Employee's Cohort study (TEC), conducted between 2018 and 2020 according to the guidelines in the Declaration of Helsinki. All employees of Tehran University of Medical Sciences (TUMS) were invited to take part in the TEC study. To inform the University personnel, official invitations were made by the university's deputy of research and the human resources management to all the faculties and centers affiliated with the university. The study's poster and brochure were also sent to TUMS' centers to present the cohort's goals and executive phases to the participants. For the overall TEC study, the primary inclusion criterion was being a permanent employee of Tehran University of Medical Sciences (TUMS). For the current analysis, all participants from the TEC baseline phase who had complete dietary and biochemical data and met the age criterion (20–50 years) were initially considered. No specific inclusion criteria were considered in the whole TEC study³⁴. However, for this study, participants with any acute or chronic disease background, such as diabetes mellitus, cancers, polycystic ovary syndrome (PCOS), hepatic, and kidney disease, were excluded. Furthermore, alcohol consumption, adherence to special/non-normal dietary intake (e.g., very low-calorie for weight loss, medically prescribed diets for conditions disease, vegetarian/vegan diets, or any other diet substantially different from the typical dietary pattern), significant body weight changes over the last year, using body weight loss and/or glucose and/or lipid-lowering medications, dietary energy intake below 800 or over 4200 (kcal/day) were considered as exclusion criteria. Considering the criteria, a total of 4027 participants were included in this study (Fig. 2). A written informed consent was obtained from all participants. This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline. The medical Ethics Committee of the TUMS Tehran, Iran, approved the study (IR.TUMS.MEDICINE.REC.1401.1064).

Assessment of dietary intakes

Usual dietary intakes were assessed using a self-administered, validated 144-item dish-based food frequency questionnaire (FFQ). Dietary intake assessment was conducted using a validated, self-administered 144-item dish-based food frequency questionnaire (FFQ). The FFQ encompassed a comprehensive list of food items, including mixed dishes (cooked or canned), grains (various bread types, cakes, biscuits, and potatoes), dairy

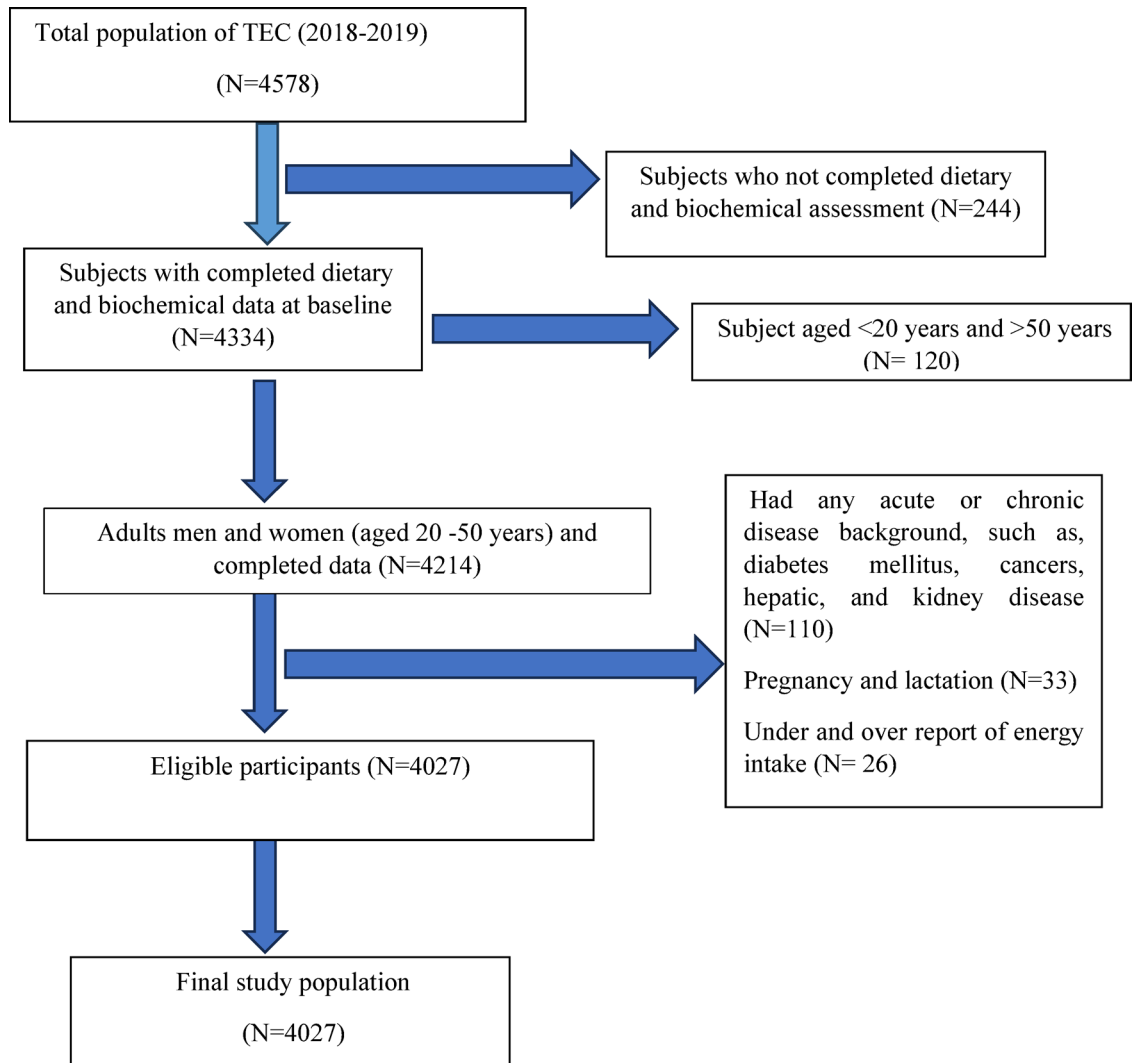


Fig. 2. Flowchart of the study population.

products (butter and cream), fruits, vegetables, and miscellaneous items such as sweets, fast foods, nuts, desserts, and beverages. Standard portion sizes were applied to quantify consumption. Participants reported their intake frequency using nine multiple-choice options, ranging from “never or less than once a month” to “6 or more times per day”. Daily nutrient intake was calculated using the US Department of Agriculture’s (USDA) National Nutrient Databank³⁵. The validity of this dish-based semi-quantitative FFQ was examined in a sample of 282 people using six 24-hour dietary recalls as well as biomarkers as the gold standard. All subjects completed two FFQs over winter and summer with a 6-month interval. The reliability was evaluated using an intra-class correlation coefficient (ICC) and validity was examined using energy-adjusted de-attenuated correlation coefficients (CC), and cross-classification analyses. De-attenuated correlation coefficients for the FFQ and the 24-hour recalls ranged between 0.32 and 0.88 (Mean = 0.59). The de-attenuated correlation coefficients between the FFQ and plasma levels of retinol and beta-carotene were 0.58 and 0.40, respectively ($P < 0.05$). Cross-classification into the same or adjacent quartiles ranged between 67.7% (for dietary fiber) and 82.6% (for Thiamin) and 5% were classified in opposite quartiles. Correlation coefficients for nutrients between two FFQs ranged between 0.4 and 0.85. This information revealed that the questionnaire could provide a reasonably valid and reliable measurement of long-term dietary intake.

Measuring dietary intakes of NO₃⁻ and NO₂⁻

Given the Iranian Food Composition Table is incomplete, and has limited data on the nutrient content of raw foods and beverages, the US Department of Agriculture Food Composition Table was used to analyze the energy and nutrient content of foods and beverages (except for NO₃⁻ and NO₂⁻)³⁶. Food composition values for NO₃⁻ and NO₂⁻ were derived from a recent survey on Iranians’ most commonly consumed foods. Briefly, the NO₃⁻ and NO₂⁻ contents of 87 food items including grains, legumes, fruits and vegetables, dairy products, meats, and processed meats were measured using validated spectrophotometric methods in the previous studies³⁷.

Assessment of biochemical indicators

After 12–14 h of overnight fasting, blood samples were taken from all participants between 08:00 and 09:30 AM. Plasmas were extracted after centrifuging the blood samples for 10 min at 3000 rpm and froze immediately for further analysis. Fasting blood sugar (FBS), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) were measured using enzymatic colorimetric assays and phosphotungstic acid methods. Serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALK) were quantified via enzymatic techniques. Analyses were performed using available commercial kits (Pars Azmoon Inc., Tehran, Iran).

Assessment of BP and heartbeat

BP was measured three times after a 20-minute rest and 2- to 4-hour rests between measurements in the sitting position from the right arm using a standardized mercury sphygmomanometer. The average of two measurements was considered as the participant's BP.

Assessment of anthropometric indices

Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. A digital scale was used to measure weight while participants wore light clothes, without shoes. Height was measured while participants stood in a normal position without shoes using a tape measure. Waist circumference (WC) was measured to the nearest 0.1 cm (at anatomical landmarks), at the middle of the lower rib margin and iliac crest, using a soft tape meter, without any pressure on the body. Hip circumference (HC) was measured using an inelastic tape measure with 0.1 cm precision at the widest part of the buttocks. Waist-hip ratio (WHR) was calculated by dividing WC by HC. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). A bioelectrical impedance analyzer (BIA) was used to measure body composition variables based on the manufacturer's protocol (Tanita MC-980MA (Seoul, Korea)).

Definition of MetS and its components

According to the diagnostic criteria proposed by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), MetS was characterized as having at least three of the metabolic abnormalities^{38,39}: (1) Hyperglycemia as FBS ≥ 100 mg/dL (5.6 mmol/L), (2) Hypertriglyceridemia as serum TG ≥ 150 mg/dL (1.69 mmol/L), (3) Low HDL-C as serum HDL-C < 40 mg/dl (1.03 mmol/l) in men and < 50 mg/dl (1.29 mmol/l) in women, (4) HTN as BP $\geq 130/85$ mmHg, and (5) Abdominal obesity as WC > 90 cm in men and > 80 cm in women. However, based on NCEP ATP III, modified for the Iranian population, we considered WC > 95 cm as abdominal obesity.

Assessment of other variables

Physical activity was assessed using the short form of the International Physical Activity Questionnaire (IPAQ) and metabolic equivalent minutes per week (MET-min/week) were calculated. The validity of IPAQ has been previously examined⁴⁰. MET scores for vigorous- and moderate-intensity activities and walking (for at least 10 min) were multiplied by the amount of time each participant spent on this activity, considering the frequency of engaging in the mentioned activity over the past week. Then, the scores for different activities were summed up to obtain the total MET-min/week. Sociodemographic characteristics including age, sex (male/female), marital status (single/married), smoking (non-smoker/smoker), nutritional supplements use (yes/no), occupational groups and socioeconomic status (SES) were collected using a self-administered questionnaire.

Statistical analysis

The normal data distribution was measured using the Kolmogorov–Simonov test (P -value > 0.05). The data were presented as number (%) for categorical variables and mean \pm standard deviation (SD) for continuous variables. An independent T-test was used to compare the continuous variables between two groups stratified by sex and having MetS. A Chi-square test was used to compare the categorical variables. Characteristics of participants over quantiles of dietary intake of NO_3^- and NO_2^- were evaluated using one-way analysis of variance (ANOVA) and analysis of covariance (ANCOVA) in crude and adjusted models, respectively. Dietary intake of NO_3^- and NO_2^- were divided into quantiles and the first category was considered the reference group. The post-hoc analysis (Bon-Ferroni) was performed to identify the significant mean difference of the variables over quantiles of NO_3^- and NO_2^- . The association between intake of NO_3^- and NO_2^- and odds of MetS and its components was assessed using logistic regression analysis. A logistic regression analysis was used to assess the median of NO_3^- and NO_2^- intake from plant and animal sources and MetS and its components. The analysis was adjusted for age, energy intake, BMI, and physical activity in model 1 and further controlled for smoking, sex, education, marriage status, SES, use of multivitamins, and vitamin C intake in model 2. Data analyses were performed using IBM SPSS (SPSS Inc., Chicago, IL, USA, version 26). A P value of < 0.05 was considered statistically significant.

Results

Study population characteristics

This cross-sectional study was conducted on 4027 adults of which, 2409 and 1618 were women and men, respectively. The mean (SD) intake of NO_3^- and NO_2^- were 663.5 (235.23) and 12.65 (4.01) mg/day, respectively. The dietary intake of NO_3^- from animal and plant sources was 19.5 (13.6) and 553 (236) mg/day, respectively. The mean intake of NO_2^- from animal and plant sources was a close amount which was 4.2 (3.6) vs. 5.5 (2.03) mg/day.

A relatively high NO_3^- concentration was observed in bread (~ 52.0 mg-100 g^{-1}). The mean (SD) of NO_3^- and NO_2^- in fruits were 49.74 (32.59) and 1.39 (0.90) mg-100 g^{-1} , respectively. The NO_2^- levels in vegetables ranged

between 0.22 and 0.73 mg·100 g⁻¹. Lettuce (375 mg·100 g⁻¹), and celery (2615 mg·100 g⁻¹) had the highest NO₃⁻ concentrations among vegetables. Mean NO₃⁻ and NO₂⁻ concentrations in meats and processed meats were 6.16–22.4 and 2.50–12.10 mg·100 g⁻¹, respectively.

Table 1 shows the participants' characteristics over the categories of MetS, stratified by sex. The mean SD (age, weight, BMI, WC, and BF, of participants were 40.72 (8.68) years, 73.93 (14.96) kg, 26.82 (4.71) kg/m², 88.37 (11.77) cm, 41.23 (5.88) %, respectively. The majority of participants were married (77%), non-smokers (58%), overweight and obese (64%), without MetS (89%), and had a college education level (73%). The prevalence of MetS was higher among females compared to males (76% vs. 24%). The mean values of weight, height, WC, HC, systolic BP (SBP), diastolic BP (DBP), FBG, total cholesterol (TC), LDL-C, TG, ALT, AST, and ALK were significantly higher in participants with MetS, while the mean FFM and HDL-C were significantly lower in participants with MetS than those without MetS ($P < 0.05$). In participants with MetS, females had significantly higher mean levels of HDL-C, weight, and WC ($P < 0.05$), while men had significantly higher levels of FBS, TG, TC, liver enzymes, SBP, and DBP ($P < 0.05$).

Characteristics and dietary intake of participants over quintiles of NO₃⁻ and NO₂⁻ intake

Characteristics and dietary intakes of participants across categories of dietary intakes of NO₃⁻ and NO₂⁻ are presented in Tables 2 and 3, respectively. Compared to the lowest quintile of intake of NO₃⁻, participants in the highest quintile, were less likely to be smokers (14% vs. 25%). The prevalence of MetS was lower in the highest quintile compared to the lowest quintile of NO₃⁻ intake (0.07% vs. 0.27%) and (10% vs. 26%) in NO₂⁻ intake. Furthermore, there was a significant difference in BF, SMM, FFM, and SBP across quintiles of NO₃⁻ and NO₂⁻ in the model, adjusted for age, sex, kcal, PA, and BMI ($P < 0.05$). A significant difference between the material, job, smoking, and education was found between quintile intake NO₂⁻ (Table 2). The intake of energy and macro and micronutrients increased over quintiles of NO₃⁻ and NO₂⁻ intake (Table 3).

The association between MetS and its components and quintiles of NO₃⁻ and NO₂⁻ intake

The association between dietary intake of NO₃⁻ and NO₂⁻ and MetS and its components are presented in Tables 4 and 5. The intake of dietary NO₃⁻ was not significantly associated with the odds of MetS in the crude model. However, after adjusting for potential confounding variables, the third quintile (584.10–684.82.10.82 mg/day) of dietary NO₃⁻ was associated with 38% (OR=0.62; 95% CI=0.38, 0.91; $P=0.02$) lower odds of MetS. However, after controlling for confounding factors, no significant association between the highest intake of NO₃⁻ (≥ 816.33 mg/day) and MetS was found (OR=0.79; 95% CI=0.47, 1.34; $P=0.39$). Also, no significant association between the intake of NO₂⁻ and the odds of MetS was observed (Table 4).

After adjusting for confounding factors, there was no significant association between dietary intake of NO₃⁻ and NO₂⁻ and the odds of hypertriglyceridemia and hyperglycemia. However, reduced levels of HDL-C were marginally significantly lower in the highest quintile of NO₃⁻ in the crude model (OR=0.88; 95% CI=0.67, 1.14, $P=0.07$), which remained significant after controlling for confounders in model 2 (OR=0.70; 95% CI=0.54, 0.90, $P=0.01$, P for trend=0.05) (Table 4).

In the full adjusted model, adults with the highest intake of NO₃⁻ had 26% and 25% reduction of odds of HTN and abdominal obesity compared to the lowest intake, respectively (OR=0.74; 95% CI=0.48, 1.02; $P=0.001$, P for trend=0.04 and OR=0.75; 95% CI=0.66, 1.66; $P=0.02$, P for trend=0.02) (Table 4).

In the adjusted model 1, high intake of NO₂⁻ was associated with lower levels of HDL-C in the fourth and fifth quintile compared to the reference group (OR=0.89; 95% CI=0.58, 1.38; $P=0.01$ and OR=0.81; 95% CI=0.61, 1.10; $P=0.03$, respectively). Furthermore, participants with the highest NO₂⁻ intake compared to the lowest quintile of dietary NO₂⁻ were 56% and 21% less likely to have HTN and abdominal obesity, respectively (Table 5).

The association between MetS and its components and quintiles of intake of NO₃⁻ and NO₂⁻ from plant and animal sources

The association between intake of NO₂⁻ and NO₃⁻ from animal and plant sources with odds of MetS and its components is presented in Table 6. Dietary intake NO₂⁻ and NO₃⁻ from plant and animal sources is divided into two groups based on median intake. After adjustment for confounders, the higher intake of NO₃⁻ from plant source, compared to lower intake, was associated with reduced odds of HTN (OR=0.87; 95% CI=0.61, 1.24, $P=0.04$), abdominal obesity (OR=0.93; 95% CI=0.76, 1.14, $P=0.01$) and low HDL-C (OR=0.90; 95% CI=0.75, 1.08, $P=0.06$). In the adjusted model, participants with a higher intake of NO₃⁻ from animal sources compared to the lower intake, were 1.53 and 1.38 times more likely to have HTN and hyperglycemia, respectively.

High intake of NO₂⁻ from animal sources increased the odds of HTN and hyperglycemia compared to low intake (OR=1.59; 95% CI=1.12, 2.25, $P=0.02$ and OR=1.21; 95% CI=0.90, 1.21, $P=0.01$). In the adjusted model, subjects with higher consumption of NO₂⁻ from plant sources had 0.08% and 21% lower odds of low HDL-C and HTN, respectively ($P < 0.05$).

HDL high-density lipoprotein, *MetS* metabolic syndrome. *MetS*-, normal values of TG, FBS, WC, BP and HDL and <median were the reference group. P -values ≤ 0.05 were considered significant. P value < 0.05 and marginal is bolded. The adjusted model the analysis was adjusted for age, energy intake, physical activity, BMI, smoking, sex, education, marriage status, SES, use of multivitamin and intake vitamin C. Median intake of Nitrate from animal and plant was 22.28 and 595.18 mg/day, respectively. The median intake of Nitrite from animal and plant sources was 6.27 and 5.62 mg/day, respectively.

Discussion

This study investigated the associations between dietary nitrate (NO₃⁻) and nitrite (NO₂⁻) intake and MetS and its individual components. The main findings of this study were that participants in the third quintile of NO₃⁻

Variables	All participants				Participants with MetS			Participants without MetS		
	Total (n = 4027)	With MetS (n = 451)	Without MetS (n = 3576)	P value	Female (n = 344)	Male (n = 107)	P value	Female (n = 2065)	Male (n = 1511)	P value
Continuous variables, mean ± SD										
Age (year)	40.72 (8.68)	40.37 (8.47)	40.81 (8.69)	0.33	40.47 (8.68)	39.66 (6.84)	0.44	40.10 (8.36)	41.78 (9.03)	<0.001
PA (MetS)	1202.06 (1075.34)	766.73 (721.12)	953.38 (1184.78)	0.32	993.10 (856.12)	981.12(1071.7)	0.55	1181.37(1280.46)	1013.23(1132.90)	0.97
Anthropometric indices										
Weight(kg)	73.93 (14.96)	81.31 (16.46)	72.92 (14.46)	<0.001	81.42 (16.22)	80.55 (18.20)	0.02	72.90 (14.60)	72.95 (14.26)	0.90
Height(cm)	165.24 (9.21)	167.177 (9.99)	164.84 (9.08)	<0.001	167.99 (9.95)	166.27 (10.25)	0.25	164.92 (9.03)	164.74 (9.15)	0.56
BMI (kg/m ²)	26.82 (4.71)	28.50 (4.36)	26.84 (4.82)	0.17	26.53 (4.45)	26.30 (3.66)	0.73	26.86 (4.87)	26.87 (4.60)	0.92
WC (cm)	88.37 (11.77)	94.99 (12.23)	87.53 (11.49)	<0.001	95.16 (12.07)	93.78 (13.35)	0.007	87.37 (11.59)	87.75 (11.35)	0.33
HC (cm)	103.39 (8.19)	106.31 (9.46)	103.04 (7.96)	<0.001	106.35 (9.60)	106.03 (8.4)	0.82	103.01 (8.03)	103.10 (7.88)	0.72
Body composition										
BF (%)	41.23 (5.88)	49.66 (4.17)	41.36 (8.19)	0.11	40.28 (3.17)	37.010 (5.18)	0.45	40.18 (4.99)	41.56 (5.12)	0.13
SMM (kg)	25.63 (3.78)	26.72 (2.89)	24.02 (4.06)	0.33	25.63 (9.07)	24.85 (4.88)	0.91	25.63 (3.72)	24.55 (3.98)	0.79
FFM (kg)	53.16 (10.89)	51.96 (10.19)	53.29 (10.59)	0.02	52.01 (10.29)	51.64 (9.61)	0.81	53.32 (10.93)	53.24 (10.98)	0.82
Blood pressure										
Systolic(mmHg)	112.52 (13.52)	117.79 (17.47)	111.94 (12.88)	<0.001	117.21 (16.95)	121.84 (20.42)	0.01	111.23 (12.71)	112.90 (13.07)	<0.001
Diastolic(mmHg)	75.13 (8.30)	77.82 (10.12)	74.83 (8.03)	<0.001	77.40 (9.93)	80.70 (11.04)	0.03	74.34 (8.02)	75.49 (7.99)	<0.001
Pulse	77.58 (8.63)	78.33 (8.81)	77.51 (8.61)	0.05	78.18 (8.83)	79.36 (8.68)	0.37	77.22 (8.50)	77.89 (8.74)	0.02
Blood parameters										
FBS (mg/dl)	86.29 (20.08)	102.54 (40.12)	84.52 (15.47)	<0.001	100.59 (37.43)	115.96 (53.76)	0.01	83.80 (13.95)	85.51 (17.29)	0.002
TC (mg/dl)	180.38 (38.71)	188.05 (39.55)	179.55 (38.54)	<0.001	186.60 (37.82)	198.02 (49.21)	0.05	179.28 (38.48)	179.92 (38.64)	0.62
HDL (mg/dl)	46.93 (10.19)	40.72 (6.46)	47.62 (10.27)	<0.001	41.18 (6.31)	37.60 (6.69)	0.001	47.81 (10.09)	47.37 (10.52)	0.21
LDL (mg/dl)	104.35 (26.24)	110.49 (28.19)	104.03 (26.09)	0.07	103.79 (27.84)	109.32 (30.37)	0.19	104.16 (25.91)	103.86 (26.33)	0.73
TG (mg/dl)	124.25 (71.74)	205.03 (97.88)	115.35 (62.33)	<0.001	197.87 (80.62)	254.34 (168.88)	0.02	112.41 (58.13)	119.37 (67.48)	0.001
ALT (IU/L)	26.65 (19.82)	36.16 (23.44)	25.15 (19.26)	<0.001	33.29 (23.77)	40.12 (20.27)	0.05	24.49 (18.99)	26.05 (19.59)	0.01
AST (IU/L)	19.36 (9.97)	21.92 (10.99)	19.11 (9.87)	<0.001	21.49 (11.02)	24.84 (10.47)	0.04	18.67 (9.07)	19.71 (10.84)	0.003
ALK (IU/L)	173.45 (50.19)	188.42 (47.61)	171.74 (50.08)	<0.001	186.10 (46.82)	204.32 (50.43)	0.01	171.07 (48.56)	172.65 (52.88)	0.35
Categorical variables, N (%)										
BMI categories										
Normal	1458 (36)	182 (40)	1298 (36)	0.48	194 (56)	48 (45)	0.76	745 (36)	612 (40.5)	0.94
Overweight	1704 (42)	189 (42)	1533 (43)		99 (29)	50 (47)		866 (42)	617 (41)	
Obesity	865 (22)	80 (18)	745 (21)		51 (15)	12 (8)		454 (22)	282 (54)	
Education levels										
≤ Diploma	1084 (27)	88 (19.5)	983 (27)	0.03	75 (22)	13 (12)	0.69	386 (18)	597 (39.5)	<0.001
University educated	2943 (73)	363 (80.5)	2593 (73)		269 (78)	94 (88)		1679 (82)	914 (60.5)	
Marriage status										
Married	3140 (77)	287 (64)	2853 (79)	0.01	242 (70)	45 (43)	0.002	1480 (70.5)	1340 (90)	<0.001
Single	887 (23)	164 (36)	723 (21)		102 (30)	62 (57)		618 (29.5)	138 (10)	
Occupation groups										
Office	1801 (44)	197 (43)	1445 (40)	0.22	159 (46)	38 (35)	0.49	893 (43)	552 (36.5)	0.80
Clinical	1318 (32)	147 (32)	1183 (33)		105 (30)	42 (39)		677 (32)	506 (33.5)	
Technical and facilities	570 (14)	77 (17)	626 (17)		53 (15)	24 (22)		304 (15)	322 (21)	
Security guard	338 (10)	30 (8)	322 (10)		27 (0.09)	3 (0.04)		191 (10)	131 (10)	
Socioeconomic status										
High	176 (4)	80 (17)	150 (5)	0.28	20 (6)	60 (56)	0.25	94 (4)	54 (4)	0.19
Moderate	3713 (92)	356 (78)	3303 (91)		313 (90)	43 (40)		1903 (93)	1402 (92)	
Low	138 (4)	15 (0.05)	123 (4)		11 (4)	4 (0.04)		66 (3)	57 (4)	
Smoking										
Yes	1695 (42)	222 (49)	1503 (43)	0.95	145 (42.5)	50 (46)	0.77	813 (39)	690 (45)	<0.001
No	2332 (58)	229 (51)	2073 (57)		199 (57.5)	57 (54)		1252 (61)	821 (55)	
Continued										

Variables	All participants				Participants with MetS			Participants without MetS		
	Total (n = 4027)	With MetS (n = 451)	Without MetS (n = 3576)	P value	Female (n = 344)	Male (n = 107)	P value	Female (n = 2065)	Male (n = 1511)	P value
Supplements use										
Yes	450 (11.2)	46 (10.3)	3177 (90.1)	0.75	40 (11)	63 (58)	0.93	255(12)	144 (1)	0.008
No	3577 (88.8)	405 (9.9)	399 (89.7)		304 (89)	44 (42)		1810 (88)	1367 (99)	

Table 1. General characteristics of study participants ($n = 4027$). *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *ALK* alkaline phosphatase, *BMI* body mass index, *BF* body fat, *FFM* free fat mass, *FBS* fasting blood sugar, *HDL* high-density lipoprotein, *HC* hip circumference, *LDL* low-density lipoprotein, *MetS* metabolic syndrome, *PA* physical activity, *SMM* skeletal muscle mass, *TBW* total body water, *TC* total cholesterol, *TG* triglyceride, *WC* waist circumference, *WHR* weight to hip ratio. Continuous variables are presented as means (\pm SD); P value obtained from the independent t-test. Categorical variables are presented as N (%). P value obtained from the chi-square analysis. P-values < 0.05 were considered significant.

had lower odds of having MetS than participants in the first quintile. Furthermore, the participants in the fifth quintile of NO_3^- and NO_2^- intake had a lower likelihood of having abdominal obesity, HTN, and lower HDL-C. However, no significant association was found between the intake of NO_3^- and NO_2^- and hypertriglyceridemia and hyperglycemia. The higher intake of NO_3^- and NO_2^- from plant sources was inversely associated with HTN, and lower HDL-C, while the higher intake of NO_3^- and NO_2^- from animal sources was positively associated with HTN and hyperglycemia.

The mean daily dietary intakes of NO_3^- and NO_2^- among participants were 663.5 mg/day and 12.65 mg/day, respectively. Furthermore, the NO_3^- intake from plant sources was higher than animal sources. In an Iranian population-based study, the mean intake of NO_3^- and NO_2^- was 455 and 9.4 mg/day, similar to our study's estimate⁴¹. However, it needs to be mentioned that due to the lack of data on NO_3^- and NO_2^- content in drinking water and individuals' water intake, NO_3^- and NO_2^- intake from drinking water were not estimated. Previous studies have indicated that the concentration of NO_3^- and NO_2^- in drinking water was below the standard limits of 50 mg/L. Considering the low amount of water intake among the Iranian population (approximately 0.96 L), NO_3^- and NO_2^- intake from drinking water in the Iranian population is relatively low^{42,43}.

Our findings indicated that participants in the third quintile of NO_3^- intake were less likely to have MetS compared to those in the lowest quintile.

Notably, the inverse association between NO_3^- intake and MetS was observed only in the third quintile (584.10–684.82 mg/day), but not in higher or lower intake categories. In line with our results, a randomized controlled study on 40 diabetic adults from the Netherlands reported that NO_3^- but not NO_2^- was inversely associated with MetS³⁰. Furthermore, a study on mice found that 18 months of a low NO_3^- diet resulted in severe MetS³¹. Several previous studies reported that a higher NO_3^- intake is associated with a healthier metabolic state^{44–48}.

This study found an inverse association between the intake of the fifth quintile of NO_3^- and NO_2^- and HTN. There is accumulating evidence of the beneficial effects of NO_3^- and NO_2^- on cardiovascular function and lowering blood pressure^{45,49–51}. Several studies reported the impact of NO_3^- and NO_2^- in decreasing blood pressure in healthy people and patients with HTN^{51–54}. The blood pressure-lowering effects of NO_3^- may be attributed to its role in promoting vasodilation and reducing vasoconstriction, platelet aggregation, and free radical generation⁵⁵. The intake of NO_3^- and NO_2^- from animal and vegetable sources was positively and negatively associated with HTN, respectively. However, the existing studies are limited and report inconsistent findings. In line with our results, a study on 1774 Greek adults assessed dietary NO_2^- and NO_3^- intake from processed meat and found that a higher intake of NO_3^- and NO_2^- from processed meat was associated with elevated DBP⁵⁶. In contrast to our findings, a study on 988 Iranian adolescents reported no significant association between NO_3^- vegetable intake and SBP and DBP⁵⁷. The lowering blood pressure effects of vegetables might be due to calcium, potassium, polyphenols, fiber, and low sodium and animal protein content. Furthermore, the NO_3^- content could serve as a physiological substance for conversion into NO_2^- , NO, which promotes vasodilation and lowers blood pressure^{58,59}. It is suggested that vegetables provide polyphenols, which increase NO production in the gastrointestinal tract and prevent NO oxidation. Polyphenols and NO_3^- are effective in lowering blood pressure⁵⁹.

The current study showed that higher intakes of NO_3^- and NO_2^- were inversely associated with abdominal obesity. The evidence on NO_3^- and NO_2^- intake about abdominal obesity is scant and mixed. In line with our findings, a study on 516 Japanese adults reported that NO_3^- plus NO_2^- concentration was inversely associated with waist circumference and waist-to-hip ratio in women⁶⁰. Furthermore, a population-based study on 16,265 American adults found a negative association between urinary NO_3^- and abdominal obesity⁶¹. On the other hand, a study on 2445 Iranian adults found a positive association between waist circumference and serum NO_3^- plus NO_2^- in women⁶². The conflict findings might be attributable to various factors. While our study included 4027 adults aged 20 years or over, Ghasemi et al. 2013 included 2445 adults. While our study measured the intake of NO_3^- and NO_2^- , Ghasemi et al. 2013 measured serum levels of NO_3^- plus NO_2^- ⁶². The negative association between NO_3^- and NO_2^- intake and abdominal obesity may be because dietary NO_3^- increases the circulating concentration of cyclic guanosine monophosphate (cGMP), which has a significant impact on energy balance in humans^{51,61}. Furthermore, the evidence shows that NO_3^- has a role in the browning of white adipose tissue⁶³. Dietary NO_3^- elevates the thermogenic gene expression of brown adipose tissue, beta-oxidation of fatty acids,

Variables	NO ₃ ⁻ (mg/day)					P value	NO ₂ ⁻ (mg/day)					P value *	
	Q1 ≤482.43 (n=849)	Q2 482.43–584.10 (n=886)	Q3 584.10–684.82 (n=856)	Q4 684.82–816.33 (n=783)	Q5 ≥816.33 (n=653)		Q1 ≤9.35 (n=880)	Q2 9.35–11.22 (n=899)	Q3 11.22–13.09 (n=842)	Q4 13.09–15.69 (n=790)	Q5 ≥15.69 (n=766)		
Continuous variables, mean ± SD													
Age (year)	41.18 (8.55)	41.94 (9.27)	41.35(8.81)	41.28) 8.86(40.85(9.10)	0.33	41.25 (8.62)	42.08 (8.97)	41.37 (9.01)	40.86 (8.97)	41.14 (9.00)	0.13	0.12
PA (MetS)	996.12(876.1)	975.12(1072.8)	1182.38(1283.4)	1015.13 (1103.1)	1013.29 (1133.9)	0.23	998.12 (896.16)	983.18 (1091.81)	953.18 (786.95)	1013.25 (1133.95)	1185.39 (1289.45)	0.41	0.47
Anthropometric indices													
Weight (kg)	73.93 (14.67)	74.19 (14.50)	72.95 (13.88)	74.01 (15.37)	73.99 (16.27)	0.55	73.97 (14.68)	73.68 (13.94)	74.18 (15.07)	73.22 (14.97)	73.98 (15.94)	0.79	0.55
Height (cm)	165.30 (9.20)	164.64 (9.48)	164.41(8.84)	165.56 (9.28)	164.94(9.68)	0.20	164.79 (9.26)	164.84 (9.12)	164.91 (9.42)	165.14 (9.18)	164.82 (9.45)	0.96	0.97
BMI (kg/m ²)	26.58 (4.38)	26.38 (4.28)	26.97(5.72)	26.87 (5.01)	26.69 (4.07)	0.45	26.64 (4.27)	26.95 (5.50)	26.80 (5.23)	26.13 (4.28)	26.43 (4.20)	0.52	0.46
WC (cm)	87.44 (11.27)	88.10 (11.70)	86.38(10.83)	87.12(11.76)	87.61(13.08)	0.08	87.50 (11.40)	87.30 (11.35)	87.74 (11.61)	86.61 (11.47)	87.38 (12.76)	0.46	0.55
HWC (cm)	103.54 (7.90)	103.82 (8.70)	103.13(7.44)	103.01(8.16)	103.56 (9.24)	0.32	103.66 (8.47)	103.36 (8.40)	103.42 (7.58)	103.10 (8.06)	103.54 (8.85)	0.79	0.72
Body composition													
BF (%)	41.2 (3.17)	40.23 (2.18)	41.25(2.18)	41.03 (2.19)	40.02 (2.19)	0.64	41.58 (2.18)	40.23 (2.28)	41.87 (2.10)	40.81 (2.18)	39.82 (2.17)	0.18	<0.001
FFM (kg)	52.34 (10.96)	53.39 (10.81)	52.18 (10.89)	53.12 (11.03)	53.4 (10.72)	0.36	53.17 (11.02)	52.91 (10.57)	52.00 (11.23)	52.79 (10.43)	53.00 (11.21)	0.97	<0.001
SMM (kg)	27.44 (7.97)	28.15(7.79)	27.80(7.90)	28.04 (8.08)	28.18 (7.74)	0.12	27.99 (7.92)	27.84 (7.79)	27.95 (8.23)	27.77 (7.56)	27.94 (8.15)	0.98	<0.001
Blood pressure													
Systolic (mmHg)	113.87 (13.67)	113.76 (14.01)	113.26 (12.64)	112.13 (13.80)	110.60 (13.84)	0.83	114.46 (13.84)	113.31 (13.08)	113.95 (14.11)	113.10 (14.19)	112.54 (12.76)	0.09	0.01
Diastolic(mmHg)	75.38 (8.62)	75.42 (8.77)	75.42 (8.25)	75.16 (8.73)	75.63 (8.61)	0.94	75.62 (8.89)	75.50 (8.35)	75.58 (9.08)	74.75 (7.88)	75.44 (8.70)	0.32	0.49
Pulse	77.19 (8.26)	77.63 (8.61)	77.40 (8.77)	77.58 (8.62)	77.53 (8.84)	0.88	77.78 (8.72)	77.34 (8.24)	77.28 (8.79)	77.42 (8.45)	77.47 (8.94)	0.84	0.87
Blood parameters													
FBS (mg/dl)	86.77 (23.67)	85.70 (20.57)	84.93 (16.81)	86.31 (21.92)	86.12 (18.14)	0.53	85.92 (22.26)	85.39 (18.26)	86.68 (22.29)	84.83 (16.32)	87.69(24.34)	0.19	0.15
TC (mg/dl)	180.64(36.49)	178.29(36)	178.95(38.02)	180.11(38.59)	177.31 (41.52)	0.61	177.71 (36.04)	181.01 (38.69)	179.53 (39.31)	178.89 (39.67)	180.49 (38.85)	0.42	0.06
HDL (mg/dl)	46.89 (9.73)	47.02 (10.07)	47.06 (10.45)	46.54 (9.75)	47.19 (10.52)	0.84	47.02 (10.15)	47.14 (9.87)	47.15 (10.54)	46.60 (9.51)	46.48 (10.36)	0.72	0.45
LDL (mg/dl)	104.38(26.22)	102.92(25)	103.78(25.35)	103.37(26.82)	101.58 (27.66)	0.52	102.82± 25.83	104.93 (25.98)	103.42 (25.76)	101.99 (27.19)	103.81 (26.09)	0.31	0.08
TG (mg/dl)	123.46(74.66)	121.62(67.6)	121.74(66.07)	128.93(83.68)	119.72 (64.95)	0.23	121.69 (74.01)	122.94 (78.52)	122.62 (70.40)	124.88 (67.70)	125.84 (67.39)	0.87	0.29
ALT (IU/L)	26.03 (19.78)	25.46 (18.58)	26.24 (18.87)	27.74 (5.27)	25.95 (19.25)	0.35	25.89 (19.13)	25.46 (20.08)	26.07 (18.50)	27.78 (24.79)	26.47 (19.25)	0.31	0.28
AST (IU/L)	19.06 (8.64)	18.67 (8.93)	19.02 (7.85)	20.85 (15.38)	18.83 (8.05)	0.001	18.90 (7.88)	19.20 (13.60)	19.56 (10.29)	19.76 (9.71)	18.99 (7.63)	0.51	0.60
ALK (IU/L)	173.71(47.37)	170.80(48.6)	170.59(47.96)	170.11(53.51)	172.93 (49.09)	0.37	172.37 (48.06)	171.93 (48.45)	170.93 (47.31)	174.06 (52.41)	174.65 (51.37)	0.70	0.85
Categorical variables, N (%)													
BMI categories													
Normal	263 (18)	267 (19)	245 (17)	246 (16)	437 (30)		301 (20)	313 (23)	313 (22)	287 (19)	244 (17)		
Overweight	346 (20)	407 (23)	415 (24)	361 (21)	175 (12)	0.47	418 (25)	397 (22)	399 (23)	334 (19)	156 (10)	0.92	0.67
Obesity	201 (24)	197 (22)	206 (23)	141 (17)	120 (14)		180 (21)	192 (22)	200 (24)	198 (22.5)	95 (10.5)		
Metabolic syndrome													
No	766 (21)	772 (22)	791 (23)	718 (20)	529 (14)	0.08	773 (21)	784 (23)	764 (21)	741 (20)	514 (15)	0.71	0.72
Yes	121 (27)	123 (27)	100 (22)	73 (17)	34 (0.07)		119 (26)	111 (24)	126 (28)	58 (12)	37 (10)		
Education levels													
≤Diploma	169 (15.5)	268 (24)	270 (25)	219 (21)	158 (14.5)	0.08	223 (20.5)	243 (22)	284 (26)	231 (21.5)	103 (10)	0.20	<0.001
University	632 (22)	601 (21)	596 (20)	579 (19)	535 (18)		416 (14)	668 (23)	683 (23)	700 (23.5)	476 (16.5)		
Continued													

Variables	NO ₃ ⁻ (mg/day)					P value	NO ₂ ⁻ (mg/day)					P value	P value *
	Q1 ≤482.43 (n = 849)	Q2 482.43–584.10 (n = 886)	Q3 584.10–684.82– 684.82–10.82 (n = 856)	Q4 684.82– 816.33–82.33 (n = 783)	Q5 ≥816.33 (n = 653)		Q1 ≤9.35 (n = 880)	Q2 9.35–11.22 (n = 899)	Q3 11.22–13.09 (n = 842)	Q4 13.09–15.69 (n = 790)	Q5 ≥15.69 (n = 766)		
Marriage status													
Married	563 (21)	575 (22)	580 (23)	529 (21)	324 (13)	0.42	191 (23)	175 (20)	177 (21)	176 (21)	125 (15)	0.75	<0.001
Single	336 (23)	324 (22.5)	316 (21)	319 (22)	161 (11.5)		666 (20)	681 (22)	681 (22)	646 (20)	509 (16)		
Occupation groups													
Office	397 (23)	377 (21.5)	356 (20.5)	371 (22)	237 (13)		398 (22.5)	399 (22.5)	359 (21)	355 (20)	260 (14)		
Clinical	311 (23)	299 (20)	267 (19)	294 (22)	210 (16)		294 (23)	299 (23)	284 (21)	262 (19)	189 (14)		
Technical and facilities	134 (23.5)	111 (19)	116 (21)	111 (19)	98 (17.5)	0.35	100 (17)	124 (21.5)	125 (20)	128 (20.5)	143 (21)	0.08	0.02
Security guard	62 (18)	79 (23)	78 (23.5)	67 (20.5)	52 (15)		86 (27)	65 (21)	43 (14)	51 (17)	63 (21)		
Socioeconomic status													
High	43 (25)	36 (21)	30 (17)	32 (18)	35 (19)		37 (21)	32 (18)	39 (22)	48 (25)	20 (14)		
Moderate	727 (19)	847 (23)	850 (23)	737 (20)	552 (15)	0.36	762 (20.5)	781 (22)	763 (20.5)	725 (19)	682 (18)	0.42	0.70
Low	29 (21)	26 (19)	26 (19)	33 (24)	24 (17)		25 (18)	22 (16)	30 (21)	36 (27)	25 (18)		
Smoking													
Yes	426 (25)	293 (17)	381 (23)	349 (21)	246 (14)	0.001	285 (22)	274 (21)	283 (22)	286 (22)	167 (13)	0.24	0.01
No	471 (20)	475 (21)	501 (22)	499 (21)	386 (16)		614 (22.7)	628 (23)	614 (22.3)	575 (21)	301 (11)		
Sex													
Female	486 (20)	493 (20.5)	485 (20)	484 (20)	461 (19.5)	0.92	348 (22)	344 (21)	326 (20)	349 (22)	218 (15)	0.58	0.35
Male	325 (20)	326 (20)	329 (20)	298 (20)	340 (22)		471 (19)	581 (24)	521 (21)	520 (21)	349 (15)		
Supplements use													
Continued													

Variables	NO ₃ ⁻ (mg/day)					NO ₂ ⁻ (mg/day)					P value	P value*	
	Q1 ≤482.43 (n = 849)	Q2 482.43–584.10 (n = 886)	Q3 584.10–684.82 (n = 856)	Q4 684.82–816.33 (n = 783)	Q5 ≥816.33 (n = 653)	Q1 ≤9.35 (n = 880)	Q2 9.35–11.22 (n = 899)	Q3 11.22–13.09 (n = 842)	Q4 13.09–15.69 (n = 790)	Q5 ≥15.69 (n = 766)			
Yes	307 (23)	297 (22)	295 (22)	204 (15)	247 (18)	206 (19)	297 (28.5)	217 (20.5)	192 (19)	138 (13)	0.44	0.66	0.06
No	592 (23)	604 (22.5)	601 (22.5)	544 (20)	336 (12)	593 (19.5)	605 (20)	681 (23)	669 (22.5)	429 (15)			0.08

Table 2. Characteristics of participants across quintiles of dietary nitrate (NO₃⁻) and nitrite (NO₂⁻) intake. *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *ALK* alkaline phosphatase, *BMI* body mass index, *BF* body fat, *FFM* free fat mass, *FBS* fasting blood sugar, *HDL* high-density lipoprotein, *HChip* circumference, *LDL* low-density lipoprotein, *MetS* metabolic syndrome, *PA* physical activity, *SMM* skeletal muscle mass, *TBW* total body water, *TC* total cholesterol, *TG* triglyceride, *WC* waist circumference, *WHR* weight to hip ratio. Continuous variables are presented as means (± SD). P value obtained from the ANOVA test. Categorical variables are presented as N (%). P value obtained from the chi-square analysis. P-value* obtained from ANCOVA test. The analysis was controlled for age, sex, energy intake, BMI and PA. α Age considered as collinear. This analysis was adjusted for sex, physical activity, and total energy intake. β Physical activity considered as collinear. This analysis was adjusted for age, sex and total energy intake. € BMI considered as collinear. This analysis was adjusted for age, sex, PA and total energy intake. † Sex considered as collinear. This analysis was adjusted for age, PA, BMI and total energy intake. P-values < 0.05 were considered significant.

Variables	Nitrate (mg/day)					Nitrite (mg/day)					P value	P value*	P value	P value*	
	Q1 ≤482.43 (n=849)	Q2 482.43–584.10 (n=886)	Q3 584.10–684.82 (n=856)	Q4 684.82–816.33 (n=783)	Q5 816.33–823.33 (n=653)	Q1 ≤9.35 (n=880)	Q2 9.35–11.22 (n=899)	Q3 11.22–13.09 (n=842)	Q4 13.09–15.69 (n=790)	Q5 ≥15.69 (n=766)					
Macronutrient															
Total (n=4027)	2674.68 (678.68)	2436.05 (454.08)	2739.31 (499.38)	3114.75 (518.48)	3506.46 (499.33)	2040.55 (434.93)	2465.00 (485.21)	2765.64 (544.72)	3110.69 (554.60)	3374.51 (606.396)	<0.0001	-	<0.0001	<0.0001	<0.0001
Energy(kcal/day)	1997.01 (416.59)	2436.05 (454.08)	2739.31 (499.38)	3114.75 (518.48)	3506.46 (499.33)	2040.55 (434.93)	2465.00 (485.21)	2765.64 (544.72)	3110.69 (554.60)	3374.51 (606.396)	<0.0001	-	<0.0001	<0.0001	<0.0001
Protein(gr/day)	69.89 (13.23)	89.00 (13.79)	103.23 (14.57)	123.99 (16.93)	146.05 (21.95)	77.02 (19.72)	92.58 (21.55)	104.96 (22.84)	117.85 (24.39)	127.50 (28.03)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Carbohydrate (gr/day)	379.58 (105.94)	355.99 (88.34)	389.36 (95.89)	432.07 (96.07)	466.35 (93.32)	284.69 (69.51)	349.80 (75.79)	395.05 (87.11)	442.93 (89.95)	472.19 (105.19)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Total fat (gr/day)	60.31 (14.50)	76.12 (16.85)	89.17 (18.06)	104.87 (22.17)	123.91 (25.56)	68.36 (20.27)	80.38 (24.08)	88.67 (24.11)	100.86 (26.64)	108.19 (28.26)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Micronutrient															
Cholesterol(gr/day)	277.60 (128.45)	240.11 (86.88)	285.63 (109.23)	327.03 (112.44)	409.52 (169.37)	214.17 (93.27)	256.28 (118.31)	316.209 (120.99)	351.01 (161.64)	286.55 (120.28)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
SFA (gr/day)	20.85 (7.38)	14.87 (4.73)	18.65 (5.64)	21.47 (6.35)	28.74 (7.96)	16.52 (5.66)	19.39 (6.95)	21.54 (6.67)	23.87 (7.32)	25.08 (7.45)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
MUFA (gr/day)	19.92 (6.66)	17.32 (3.99)	20.38 (4.35)	24.06 (5.18)	28.79 (6.36)	15.65 (4.81)	18.36 (5.95)	20.26 (5.82)	22.99 (6.42)	24.79 (6.86)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
PUFA (gr/day)	32.21 (11.42)	28.07 (7.87)	32.82 (7.92)	38.99 (10.07)	45.79 (11.23)	25.34 (8.63)	29.82 (9.91)	32.38 (9.69)	37.34 (11.66)	40.12 (12.07)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Total fiber(gr/day)	17.79 (5.97)	15.79 (3.44)	17.88 (3.71)	20.91 (5.06)	25.38 (7.67)	12.24 (3.04)	15.57 (3.11)	17.71 (3.26)	20.79 (3.71)	27.08 (6.91)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Minerals															
Phosphor (mg/day)	1165.64 (418.63)	776.72 (228.82)	1001.81 (273.39)	1186.35 (264.27)	1752.13 (374.60)	882.92 (334.81)	104.13 (341.44)	1176.98 (338.27)	1342.38 (377.47)	1576.29 (416.10)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Magnesium (mg/day)	234.87 (77.80)	159.07 (40.00)	202.66 (40.23)	237.84 (44.61)	352.18 (74.77)	171.80 (50.77)	208.74 (53.74)	233.61 (55.22)	270.39 (59.95)	340.23 (78.23)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Zinc(mg/day)	7.67 (2.58)	5.12±1.27	6.61 (1.46)	7.81 (1.52)	11.58 (2.23)	5.85 (1.96)	6.92 (2.03)	7.78 (2.15)	8.81 (2.30)	10.26 (2.58)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Copper(mg/day)	1.20 (0.67)	0.79 (0.31)	1.02 (0.41)	1.22 (0.47)	1.77 (0.51)	0.89 (0.41)	1.07 (0.46)	1.20 (0.97)	1.40 (0.56)	1.66 (0.53)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Calcium(mg/day)	936.89 (362.13)	697.37 (226.54)	867.48 (269.57)	1118.35 (329.77)	1333.29 (448.39)	721.76 (285.26)	870.39 (288.98)	998.17 (283.22)	1106.53 (332.20)	1274.10 (427.19)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Iron(mg/day)	19.86 (5.76)	14.93 (4.00)	18.18 (4.39)	20.26 (4.94)	25.75 (4.49)	14.92 (3.89)	18.05 (4.03)	20.54 (4.88)	23.38 (5.15)	25.05 (5.18)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Sodium(mg/day)	3184.40 (949.79)	2263.41 (485.64)	2805.02 (508.96)	3757.72 (697.05)	4528.75 (935.48)	2560.03 (685.89)	2926.08 (725.38)	3229.93 (804.42)	3639.97 (914.43)	3945.14 (1080.88)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Potassium (mg/day)	2971.47 (1092.29)	1931.17 (509.23)	2521.64 (479.29)	2986.83 (576.89)	4641.30 (1264.05)	2036.76 (605.41)	2544.97 (620.34)	2942.30 (667.13)	3469.43 (723.69)	4672.95 (1201.12)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Selenium (mg/day)	0.02 (0.02)	0.01 (0.01)	0.02 (0.02)	0.03 (0.02)	0.04 (0.02)	0.02 (0.02)	0.02 (0.02)	0.02±0.01	0.03±0.02	0.03±0.02	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Mn (mg/day)	2.33 (0.71)	1.72 (0.43)	2.08 (0.48)	2.37 (0.48)	3.25 (0.70)	1.77 (0.52)	2.13±0.51	2.32±0.49	2.66±0.60	3.20±0.71	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Vitamins															
A (IU/day)	1782.33 (1623.74)	989.66 (637.68)	1366.57 (843.56)	1765.38 (1227.76)	3276.25 (2600.47)	934.14 (607.86)	1369.59 (876.95)	1630.46 (1248.04)	2113.80 (1299.88)	3806.20 (2802.78)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
D(µg/day)	1.37 (1.16)	0.94 (0.85)	1.21 (1.00)	1.43 (1.10)	52.02 (1.66)	1.04 (0.94)	1.30 (1.10)	1.36 (1.05)	1.54 (1.25)	1.83 (1.46)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
E(mg/day)	3.15 (1.10)	2.24 (0.59)	2.80 (0.68)	3.20 (0.77)	4.55 (1.34)	2.85 (0.64)	2.82 (0.71)	3.12 (0.79)	3.59 (0.83)	4.65 (1.35)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
K (mg/day)	152.26 (75.22)	106.21 (45.48)	135.12 (53.21)	152.76 (45.95)	229.38 (113.58)	100.07 (48.24)	128.20 (46.87)	152.74 (50.50)	178.06 (58.52)	247.31 (106.71)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
B1(mg/day)	2.17 (0.58)	1.73 (0.44)	2.04 (0.48)	2.24 (0.54)	2.64 (0.49)	1.64 (0.38)	2.02 (0.41)	2.27 (0.49)	2.53 (0.52)	2.63 (0.57)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
B2(mg/day)	1.70 (0.67)	1.12 (0.34)	1.45 (0.39)	1.73 (0.43)	2.05 (0.66)	1.27 (0.47)	1.51 (0.50)	1.74 (0.68)	1.95 (0.59)	2.33 (0.71)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
B3(mg/day)	27.69 (7.87)	19.98 (4.66)	24.86 (5.11)	28.28 (5.80)	37.73 (6.11)	20.86 (5.20)	25.35 (5.69)	28.75 (6.82)	32.50 (6.83)	34.44 (7.24)	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Continued

Variables	Nitrate (mg/day)					Nitrite (mg/day)					P value	P value*			
	Total (n = 4027)	Q1 ≤482.43 (n = 849)	Q2 482.43– 584.10 (n = 886)	Q3 584.10– 684.82,10.82 (n = 856)	Q4 684.82– 816.33,82.33 (n = 783)	Q5 ≥816.33 (n = 653)	P value	P value*	Q1 ≤9.35 (n = 880)	Q2 9.35–11.22 (n = 899)			Q3 11.22–13.09 (n = 842)	Q4 13.09–15.69 (n = 790)	Q5 ≥15.69 (n = 766)
B6(mg/day)	1.38 (0.58)	0.91 (0.39)	1.16 (0.32)	1.40 (0.41)	1.68 (0.47)	2.14 (0.63)	<0.0001	<0.0001	0.97 (0.44)	1.21 (0.42)	1.38 (0.48)	1.62 (0.48)	2.06 (0.58)	<0.0001	<0.0001
B9(µg/day)	286.54 (105.70)	196.369 (55.80)	250.04 (64.32)	288.60 (65.92)	341.60 (94.13)	424.99 (120.47)	<0.0001	<0.0001	195.75 (61.53)	247.18 (62.78)	285.23 (70.22)	335.02 (73.13)	445.05 (110.56)	<0.0001	<0.0001
B8 (mg/day)	21.21 (7.31)	15.61 (4.83)	19.07 (5.15)	21.84 (6.16)	24.21 (6.05)	29.85 (8.39)	<0.0001	<0.0001	16.49 (5.33)	19.77 (6.35)	21.47 (6.19)	23.89 (6.61)	27.42 (8.50)	<0.0001	<0.0001
B12 (µg/day)	3.19 (6.09)	2.23 (1.71)	3.13 (2.39)	4.04 (3.75)	5.29 (11.36)	6.53 (4.85)	<0.0001	<0.0001	2.94 (2.47)	3.31 (2.64)	4.31 (4.02)	4.58 (4.29)	5.56 (4.55)	<0.0001	<0.0001
†C (mg/day)	117.16 (59.86)	75.45 (27.81)	99.67 (31.80)	116.94 (38.21)	141.10 (55.15)	187.32 (95.08)	<0.0001	<0.0001	71.92 (29.04)	95.83 (28.19)	112.95 (32.13)	139.77 (37.23)	208.37 (91.19)	<0.0001	<0.0001

Table 3. Dietary intake of participants across quintiles of nitrate (NO₃⁻) and nitrite (NO₂⁻) intake. MUFA monounsaturated fatty acid, PUFA polyunsaturated fatty acid, SFA saturated fatty acid. All data are presented as mean (±SD). P–value* The analysis was controlled for energy intake. P–value obtained from ANOVA test. P values < 0.05 were considered significant.

Variables	NO ₃ ⁻ (mg/day)													
	Q2 482.43–584.10.43.10			Q3 584.10–684.82.10.82			Q4 684.82–816.33.82.33			Q5 ≥816.33				
	OR	95%CI	P value	OR	95%CI	P value	OR	95%CI	P value	OR	95%CI	P value	P trend	
MetS+	Crude	1.06	0.72–1.43.72.43	0.91	0.65	0.44–0.95.44.95	0.10	1.11	0.78–1.57.78.57	0.53	0.86	0.56–1.32.56.32	0.50	0.51
	Model 1	1.10	0.69–1.43.69.43	0.99	0.65	0.41–0.95.41.95	0.02	1.04	0.68–1.60.68.60	0.84	0.79	0.47–1.33.47.33	0.38	
	Model 2	0.99	0.60–1.42.60.42	0.97	0.62	0.38–0.91.38.91	0.02	1.03	0.67–1.58.67.58	0.87	0.79	0.47–1.34.47.34	0.39	
Components of MetS														
Hypertriglyceridemia	Crude	1.08	0.79–1.29.79.29	0.91	0.99	0.77–1.27.77.27	0.95	1.14	0.89–1.46.89.46	0.28	1.06	0.79–1.42.79.42	0.65	0.81
	Model 1	0.97	0.77–1.28.77.28	0.97	0.94	0.72–1.24.72.24	0.70	1.07	0.79–1.44.79.44	0.65	0.97	0.68–1.38.68.38	0.87	
	Model 2	0.99	0.76–1.28.76.28	0.95	0.95	0.72–1.25.72.25	0.74	1.08	0.80–1.46.80.46	0.60	0.88	0.69–1.40.69.40	0.95	
Abdominal obesity	Crude	0.94	0.72–1.23.72.23	0.66	1.15	0.91–1.44.91.44	0.14	0.84	0.67–1.06.67.06	0.22	0.82	0.99–1.54.99.54	0.05	0.02
	Model 1	1.06	0.76–1.47.76.47	0.70	1.28	0.97–1.69.97.69	0.47	0.91	0.70–1.17.70.17	0.06	0.88	0.70–1.62.70.62	0.03	
	Model 2	1.06	0.77–1.48.77.48	0.69	1.20	0.95–1.66.95.66	0.48	0.91	0.79–1.20.79.20	0.08	0.75	0.66–1.66.66.66	0.02	
Hyperglycemia	Crude	0.81	0.55–1.18.55.18	0.27	0.78	0.53–1.14.53.14	0.21	0.82	0.56–1.21.56.21	0.33	0.99	0.70–1.63.70.63	0.73	0.60
	Model 1	0.77	0.52–1.13.52.13	0.19	0.70	0.46–1.07.46.07	0.10	0.70	0.44–1.12.44.12	0.13	0.88	0.52–1.50.52.50	0.65	
	Model 2	0.75	0.51–1.12.51.12	0.16	0.71	0.46–1.08.46.08	0.11	0.72	0.45–1.15.45.15	0.17	0.91	0.53–1.54.53.54	0.72	
HTN	Crude	0.88	0.78–1.93.78.93	0.37	1.22	0.76–1.90.76.90	0.44	0.92	0.63–1.30.63.30	0.36	0.88	0.59–1.10.59.10	0.14	0.04
	Model 1	0.75	0.76–1.96.76.96	0.39	0.99	0.73–2.01.73.01	0.43	0.95	0.68–1.26.68.26	0.22	0.76	0.48–1.15.48.15	0.05	
	Model 2	0.78	0.74–1.91.74.91	0.46	1.12	0.73–2.04.73.04	0.14	0.84	0.67–1.06.67.06	0.22	0.74	0.48–1.02	0.03	
Low HDL	Crude	0.94	0.76–1.16.76.16	0.61	0.90	0.73–1.11.73.11	0.33	0.93	0.73–1.18.73.18	0.48	0.88	0.67–1.14.67.14	0.07	0.05
	Model 1	0.96	0.74–1.14.74.14	0.44	0.97	0.67–1.06.67.06	0.16	0.92	0.70–1.20.70.20	0.22	0.87	0.65–1.09.65.09	0.05	
	Model 2	0.92	0.74–1.15.74.15	0.50	0.95	0.67–1.07.67.07	0.17	0.84	0.66–1.07.66.07	0.17	0.70	0.54–0.90.54.90	0.01	

Table 4. Association between dietary nitrate (NO₃⁻) intake and the odds of metabolic syndrome (MetS) and its components. HDL high-density lipoprotein, MetS metabolic syndrome, HTN hypertension. MetS, normal values of TG, FBS, WC, BP and HDL and Q1 intake of Nitrate <482.43 mg/day were the reference group. P-values ≤ 0.05 were considered significant. P value <0.05 and marginal is bolded. Model 1: adjusted for age, energy intake, physical activity, BMI, and Model 2: further adjustment for smoking, sex, education, marriage status, SES, use of multivitamin and intake vit C.

Variables	NO ₂ (mg/day)													
	Q2 9.35–11.22,35.22			Q3 11.22–13.09,22.09			Q4 13.09–15.69,09.69			Q5 ≥15.69				
	OR	95%CI	P value	OR	95%CI	P value	OR	95%CI	P value	OR	95%CI	P value		
MetS	Crude	0.94	0.73–1.21,73.21	0.66	1.04	0.85–1.33,85.33	0.74	0.98	0.93–1.66,93.66	0.13	1.03	0.81–1.33,81.33	0.76	0.46
	Model 1	0.85	0.58–1.25,58.25	0.42	1.05	0.71–1.57,71.57	0.78	0.80	0.53–1.68,53.68	0.86	0.84	0.52–1.34,52.34	0.47	
	Model 2	0.88	0.60–1.29,60.29	0.52	1.09	0.73–1.62,73.62	0.66	0.75	0.55–1.74,55.74	0.95	0.85	0.53–1.37,53.37	0.52	
Components of MetS														
Hypertriglyceridemia	Crude	1.24	0.93–1.66,93.66	0.13	1.04	0.81–1.33,81.33	0.74	1.03	0.81–1.33,81.33	0.76	0.94	0.73–1.12,73.12	0.66	
	Model 1	1.21	0.82–1.78,82.78	0.33	1.03	0.76–1.35,76.35	0.83	1.02	0.73–1.38,73.38	0.96	0.83	0.82–1.21,82.21	0.61	0.30
	Model 2	1.24	0.84–1.83,84.83	0.26	1.04	0.79–1.38,79.38	0.74	1.03	0.75–1.42,75.42	0.81	0.78	0.73–1.23,73.23	0.72	
Abdominal obesity	Crude	0.98	0.78–1.22,78.22	0.86	1.06	0.85–1.32,85.32	0.58	0.86	0.69–1.09,69.09	0.22	0.81	0.61–1.06,61.06	0.13	
	Model 1	1.08	0.79–1.26,79.26	0.15	1.07	0.83–1.38,83.38	0.58	0.86	0.64–1.15,64.15	0.33	0.80	0.55–1.16,55.16	0.10	0.04
	Model 2	0.99	0.78–1.25,78.25	0.96	1.06	0.83–1.37,83.37	0.60	0.84	0.63–1.12,63.12	0.25	0.79	0.50–1.15,50.15	0.02	
Hyperglycemia	Crude	0.91	0.61–1.35,61.35	0.66	1.11	0.76–1.63,76.63	0.55	0.93	0.63–1.39,63.39	0.75	1.34	0.91–1.24,91.24	0.12	
	Model 1	0.93	0.62–1.41,62.41	0.75	1.14	0.74–1.74,74.74	0.54	0.97	0.59–1.60,59.60	0.91	1.27	0.81–2.65,81.65	0.19	0.25
	Model 2	0.85	0.63–1.44,63.44	0.83	1.18	0.77–1.81,77.81	0.44	1.09	0.61–1.66,61.66	0.97	1.23	0.84–2.78,84.78	0.15	
HTN	Crude	0.81	0.52–1.26,52.26	0.36	1.12	0.74–1.70,74.70	0.57	1.08	0.65–1.78,65.78	0.75	0.54	0.32–0.89,32.89	0.01	
	Model 1	0.73	0.46–1.16,46.16	0.19	0.96	0.59–1.54,59.54	0.07	0.78	0.39–1.57,39.57	0.50	0.42	0.22–0.79,22.79	0.01	0.02
	Model 2	0.75	0.47–1.20,47.20	0.23	0.99	0.61–1.62,61.62	0.99	0.83	0.41–1.67,41.67	0.61	0.44	0.24–0.83,24.83	0.03	
Low HDL	Crude	0.99	0.75–1.15,75.15	0.52	0.97	0.65–1.10,65.10	0.81	0.89	0.59–1.35,59.35	0.12	0.82	0.60–1.13,60.13	0.11	
	Model 1	0.90	0.72–1.13,72.13	0.37	0.91	0.67–1.12,67.12	0.43	0.89	0.58–1.38,58.38	0.01	0.81	0.61–1.10,61.10	0.03	0.04
	Model 2	0.90	0.72–1.12,72.12	0.38	0.98	0.69–1.22,69.22	0.46	0.74	0.66–1.34,66.34	0.04	0.78	0.57–1.08,57.08	0.04	

Table 5. Association between dietary nitrite (NO₂⁻) intake and the odds of metabolic syndrome (MetS) and its components. HDL high-density lipoprotein, HTN hypertension, MetS metabolic syndrome. MetS-, normal values of TG, FBS, WC, BP and HDL and Q 1 intake of Nitrite < 9.35 mg/day were the reference group. P-values ≤ 0.05 were considered significant. P value < 0.05 and marginal is bolded. Model 1 :adjusted for age, energy intake, physical activity, BMI. Model 2 :further adjustment for smoking, sex, education, marriage status, SES, use of multivitamin and intake vit C.HDL high-density lipoprotein, HTN hypertension, MetS metabolic syndrome. MetS-, normal values of TG, FBS, WC, BP and HDL and Q 1 intake of Nitrite < 9.35 mg/day were the reference group. P-values ≤ 0.05 were considered significant. P value < 0.05 and marginal is bolded. Model 1 :adjusted for age, energy intake, physical activity, BMI. Model 2 :further adjustment for smoking, sex, education, marriage status, SES, use of multivitamin and intake vit C.

Variables	NO ₃ ⁻ (mg/day)						NO ₂ ⁻ (mg/day)						
	Models	Animal			Plant			Animal			Plant		
		OR	95%CI	P	OR	95%CI	P value	OR	95%CI	P value	OR	95%CI	P value
MetS +	Crude	1.07	0.84–1.36.84.36	0.56	0.92	0.72–1.17.72.17	0.50	1.08	0.85–1.37.85.37	0.51	0.91	0.71–1.16.71.16	0.45
	Adjust	1.13	0.86–1.48.86.48	0.37	0.89	0.66–1.19.66.19	0.44	1.09	0.82–1.44.82.44	0.54	0.85	0.63–1.14.63.14	0.28
Hypertention	Crude	1.39	1.03–1.88.03.88	0.03	0.88	0.65–1.18.65.18	0.05	1.39	1.03–1.88.03.88	0.03	0.97	0.72–1.30.72.30	0.08
	Adjust	1.53	1.09–2.15.09.15	0.01	0.87	0.61–1.24.61.24	0.04	1.59	1.12–2.25.12.25	0.02	0.92	0.64–1.33.64.33	0.04
Hyperglycemia	Crude	1.33	1.03–1.72.03.72	0.02	0.96	0.75–1.24.75.24	0.79	1.20	0.93–1.55.93.55	0.15	0.93	0.72–1.20.72.20	0.60
	Adjust	1.38	1.04–1.84.04.84	0.02	0.88	0.64–1.19.64.19	0.42	1.21	0.90–1.63.90.63	0.01	0.97	0.71–1.33.71.33	0.87
Abdominal obesity	Crude	0.92	0.79–1.07.79.07	0.30	0.89	0.76–1.03.76.03	0.13	1.07	0.92–1.24.92.24	0.34	0.93	0.80–1.08.80.08	0.38
	Adjust	1.04	0.83–1.20.83.20	0.96	0.93	0.76–1.14.76.14	0.01	1.07	0.83–1.21.83.21	0.93	0.96	0.79–1.17.79.17	0.12
Low HDL	Crude	0.93	0.81–1.07.81.07	0.35	0.93	0.81–1.07.81.07	0.07	1.02	0.88–1.17.88.17	0.77	0.89	0.77–1.02.77.02	0.11
	Adjust	1.07	0.91–1.28.91.28	0.38	0.90	0.75–1.08.75.08	0.06	1.02	0.85–1.21.85.21	0.82	0.79	0.65–0.95.65.95	0.01
Hypertriglyceridemia	Crude	1.10	0.93–1.29.93.29	0.25	1.02	0.87–1.20.87.20	0.75	1.01	0.86–1.19.86.19	0.85	0.97	0.83–1.15.83.15	0.78
	Adjust	1.06	0.89–1.28.89.28	0.47	0.95	0.78–1.16.78.16	0.63	1.09	0.90–1.31.90.31	0.37	0.89	0.73–1.09.73.09	0.26

Table 6. Association between dietary nitrate (NO₃⁻) and nitrite (NO₂⁻) intake from plant and animal sources and the odds of metabolic syndrome (MetS) and its components. *HDL* high-density lipoprotein, *MetS* metabolic syndrome. MetS-, normal values of TG, FBS, WC, BP and HDL and < median were the reference group. P-values ≤ 0.05 were considered significant. P value <0.05 and marginal is bolded. The adjusted model: the analysis was adjusted for age, energy intake, physical activity, BMI, smoking, sex, education, marriage status, SES, use of multivitamin and intake vitamin C. Median intake of Nitrate from animal and plant was 22.28 and 595.18 mg/day, respectively. The median intake of Nitrite from animal and plant sources was 6.27 and 5.62 mg/day, respectively.

and oxygen consumption in adipocytes¹⁷. In addition, this study reported that NO₃⁻ intake from plant sources was associated with a lower likelihood of abdominal obesity. It might be explained by the fact that vegetables have the highest NO₃⁻ content and have been consistently reported to decline the risk of obesity⁶⁴.

While this study demonstrated an inverse association between NO₃⁻ and NO₂⁻ intake and low HDL-C levels, no significant relationship was observed with hypertriglyceridemia. It should be noted that the current evidence on associations between NO₃⁻ and NO₂⁻ intake and lipid profile is mixed. Regarding the association with HDL-C, while, a study on 516 adults from Japan found a negative association between NO concentration and lower HDL-C in men⁶⁰, a study on 116 Armish adults reported a negative association between NO₂⁻ and HDL-C¹³ and a study on 988 Iranian adolescents found no significant association between NO₃⁻ intake and HDL-C⁵⁷. Regarding the association with triglyceride, in contrast to our results, a study on 988 Iranian adolescents reported an inverse association between NO₃⁻ intake and triglyceride⁵⁷. The discrepancies might be due to various sample sizes and participants' characteristics, resulting in inconsistent evidence. Furthermore, our study found that NO₃⁻ and NO₂⁻ intake from plant sources was inversely linked to lower HDL-C levels. While a study on 988 Iranian adolescents reported no significant association between NO₃⁻ vegetable intake and HDL-C⁵⁷. The evidence suggests that the NO₃⁻ content of vegetables may inhibit the increased levels of markers of oxidative stress and lipid peroxidation^{49,65}. The effect might be related to the antioxidant properties, which could decrease oxidative stress⁶⁶.

Our study found no significant association between dietary NO₂⁻ and NO₃⁻ intake and hyperglycemia. The intake of NO₂⁻ and NO₃⁻ from animal sources was positively linked to hyperglycemia. The existing evidence on this association is not consistent. While a study on 988 Iranian adolescents found no significant association between fasting blood glucose (FBS) and NO₃⁻ intake⁵⁷, a previous study on mice reported that a higher intake of NO₃⁻ was associated with a decrease in serum glucose⁶⁵. Furthermore, a study on mice reported that 3 months of low NO₂⁻/NO₃⁻ diet increased glucose intolerance compared to a regular diet³¹. The conflict in results could be due to different sample sizes, participants, and study methodology included in these studies. The mechanism might be related to the regulation of proton leak, in which adenine nucleotide translocase (ANT) and uncoupling protein 3 (UCP3) are downregulated after nitrate supplementation⁶⁷. The activation of AMP-activated protein kinase (AMPK) and GLUT4 translocation has been observed. It has also been found that long-term oral nitrate intake is accompanied by lower hyperglycemia and strong activation of AMPK in skeletal muscle in obese ZSF1 rats⁶⁸. In human studies, AMPK activation was elevated after 12 weeks of nitrate supplementation. AMPK enhances GLUT4 translocation and glucose uptake⁶⁹. Therefore, improved glucose clearance, better insulin sensitivity, and decreased Interleukin 1 beta (IL-1β) could be proposed⁷⁰. It is suggested that this translocation is due to activation of SIRT3⁶⁸.

This study found different NO₂⁻ and NO₃⁻ effects from animal and plant sources on MetS components. It should be considered that other bioactive components of plant sources such as polyphenols and antioxidants, could be involved in their protective effects. Vitamin C in plant sources could inhibit nitrosamine formation⁷¹. A study reported that a higher risk of diabetes was associated with higher and lower NO₂⁻ and vitamin C intakes, respectively⁷². It has been previously suggested that animal sources of NO₃⁻ and NO₂⁻, particularly those found in processed meats, have negative impacts on health compared to NO₃⁻ and NO₂⁻ derived from plant-based sources⁷³. Origination of nitrate and nitrite from plant or animal sources are similar. However, the contents of

some nutrients such as vitamin C in plants or amines in animal foods, lead to different consequences in humans' bodies. Based on the evidence, high nitrosamine levels that could be accompanied by lower vitamin C status cause disrupted insulin signaling⁷⁴. On the other hand, lowering nitrite's effect on blood pressure requires an acidic environment that may be provided by vitamin C⁷⁵.

This study has several limitations that should be considered when interpreting the findings. First, the cross-sectional design of our study inherently prevents the establishment of causal relationships between dietary nitrate and nitrite intake and MetS. Second, dietary data were collected using a FFQ, which is subject to recall bias and measurement error. Furthermore, responses to questions may be influenced by social desirability bias, where participants might have provided answers they perceived as more socially acceptable. Third, our study population consisted of employees of a medical sciences university, who are likely more health-conscious than the general Iranian population. This potential selection bias may limit the generalizability (external validity) of our findings to other socio-demographic groups. Fourth, the content of NO₃⁻ and NO₂⁻ in drinking water was not estimated. As mentioned above, the water intake of the Iranian population is relatively low. Fifth, the interaction of NO₃⁻ and NO₂⁻ with other nutrients, was not measured, which may have impacted the results. As a result, future prospective research is needed to confirm our findings.

Conclusion

The present study found an inverse association between the occurrence of abdominal obesity, HTN, and low HDL-C associated with the highest level of NO₃⁻ and NO₂⁻ intake compared to the lowest intake. While there was no significant association between NO₂⁻ intake and MetS, the third quintile of NO₃⁻ intake was inversely linked to MetS. Furthermore, negative and positive associations between the components of MetS and the NO₃⁻ and NO₂⁻ intake from plant and animal sources were observed, respectively. Further human clinical trials and prospective studies with long-term follow-up are needed to further investigate the potential effects.

Data availability

The data that support the findings of this study are available from Dr.Khadijeh Mirzaei but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Dr.Khadijeh Mirzaei.

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Author contributions

AM and HA contributed to the conception and design. FP and PK contributed to all experimental work, and AK contributed to data and statistical analysis. MM and KhM supervised the whole project. All authors performed editing and approved the final version of this paper for submission, also participated in the finalization of the manuscript, and approved the final draft. All authors read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

The study protocol was approved by the ethics committee of the Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1401.064) and is acknowledged by the authors. All participants signed a written informed consent.

Consent for publication

All authors performed editing and approved the final version of this paper for submission, also participated in the finalization of the manuscript, and approved the final draft.

Additional information

Correspondence and requests for materials should be addressed to A.M. or K.M.

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