Peng et al. BMC Public Health (2025) 25:234
https://doi.org/10.1186/s12889-025-21419-x

BMC Public Health

RESEARCH Open Access

Inverse relationship of oxidative balance score with hyperuricemia among Chinese adults: a population-based cross-sectional study

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Abstract

Background The oxidative balance score (OBS) is a composite metric highlights pro-oxidants and antioxidants balance, representing the overall burden of oxidative stress. This study aims to examine the association between OBS and hyperuricemia in a Chinese population.

Methods This study was based on population-based cross-sectional survey data of Fujian province from August 2020 to April 2021. OBS was determined based on 10 food and lifestyle OBS components. The association between OBS and hyperuricemia was investigated using logistic regression analysis. Subgroup analyses identified sensitive populations. Restricted cubic spline (RCS) was performed to examine the potential dose-response relationship.

Results A total of 9464 participants were included in the final analysis. An inverse association between OBS and hyperuricemia was observed and remained after adjusting for potential confounders. Each additional unit of OBS was associated with a 4% and 7% reduction in the risk of hyperuricemia in men [OR: 0.96(0.94,0.99)] and women [OR: 0.93(0.90,0.96)], respectively. Participants in the highest quartile had a 22% and 37% lower risk of hypertension compared with the lowest quartile of OBS in men [0.78(0.62,0.97)] and women [OR: 0.63(0.49,0.79)], respectively. There were significant interactions between OBS and gender, hypertension, and dyslipidemia on hyperuricemia ($P_{interaction} <$ 0.05), except for age, education, and diabetes ($P_{interaction} >$ 0.05). A linear dose-response relationship between OBS and the risk of hyperuricemia ($P_{nonlinear} = 0.7854$) was observed.

Conclusions An inverse association as well as dose-response relationship between OBS and hyperuricemia were observed. Increasing antioxidant levels through lifestyle modification may be an effective way to prevent hyperuricemia, especially in women. Large prospective cohort studies and randomized controlled trials are required to verify the effect of OBS on hyperuricemia and elucidate its causal mechanism.

Key words Oxidative balance score, Hyperuricemia, Food, Lifestyle, Dose-response

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Introduction

Uric acid is a metabolite of purines in the body, and blood levels of uric acid reflect dietary intake of purines, synthesis of uric acid by xanthine oxidase, and excretion of uric acid [1, 2]. Hyperuricemia is a chronic disease resulting from an imbalance in the balance of uric acid metabolism, characterized by abnormally elevated serum uric acid levels (≥ 7 mg/dL in men, ≥ 6 mg/dL in women, and ≥ 5.5 mg/dL in children and teenagers) [3]. Global prevalence of hyperuricemia is on a gradual rise and the prevalence of hyperuricemia ranges from 5 to 25% in different countries [4–6]. Zhang et, al [7] uncovered that hyperuricemia prevalence among Chinese adults was estimated to be 11.1% in 2015–2016 and 14% in 2018–2019, showing a significant escalating trend. Hyperuricemia is an important cause of gout, an arthritis characterized by elevated serum uric acid level, recurrent acute arthritis, and chronic tophaceous gout [8]. Previous studies showed that hyperuricemia significantly increased the risk of coronary heart disease [9, 10] and chronic kidney disease [11, 12]. These highlight a serious concern for the future and the growing health burden of hyperuricemia.

The pathogenesis of hyperuricemia is not well characterized. Dietary factors and lifestyle play important roles in hyperuricemia. Li et, al. presented a diet rich in anthocyanins and flavanones had significantly lower incidence of hyperuricemia [13]. Other studies showed that higher mushroom consumption is significantly associated with lower incidence of hyperuricemia [14, 15]. Smoking, hypertension, alcohol drinking, dyslipidemia, abdominal obesity, and physical activity were also found to be associated with the development of hyperuricemia [16–19]. Most researches mainly focused on the influence of single dietary or lifestyle factors on hyperuricemia. However, for individuals, it is often the result of the comprehensive action of multiple factors. It is more beneficial to formulate prevention and control strategies and measures to explore the influence of the comprehensive multi-factor on hyperuricemia.

Diet as well as lifestyle were also important in regulating oxidative stress [20, 21]. Multiple studies demonstrated that oxidative stress is closely associated with hyperuricemia [22, 23]. Oxidative stress is a pathological state characterized by a disruption of the balance between pro-oxidant and antioxidant factors, with pro-oxidant factors predominating. This imbalance can cause cell and tissue damage, leading to inflammation, cellular damage and various diseases [24].

The oxidative balance score (OBS) is a composite metric that highlights the overall balance of pro-oxidants and antioxidants in the diet and lifestyle, representing the overall burden of oxidative stress [25, 26]. Generally, a higher OBS indicates a lower exposure to oxidants as well as a higher exposure to antioxidants. Growing evidences have suggested that OBS was inversely associated with several diseases, including diabetes [27], cardiovascular diseases [28], chronic kidney disease [29], and nonalcoholic fatty liver disease [30]. Furthermore, several recent researches from National Health and Nutrition Examination Survey (NHANES) have found an inverse correlation between OBS and hyperuricemia [31–33]. Nevertheless, all three studies were based on the NHANES database, and these associations in other populations are yet unclear. Therefore, this study aims to examine the association between OBS and hyperuricemia in a Chinese population, which may contribute new insights for future research on the prevention and treatment of hyperuricemia or related health problems.

Materials and methods

Study population

This study was based on a Cross-sectional survey data of Fujian province from August 2020 to 2021 April. As shown in Fig. 1, participants are permanent residents who are 18 years of age or older and reside in the administrative districts of Fujian Province. Exclusion criteria for the study population were as follows: (1) participants with partially missing data; (2) participants were pregnant or lactating; and (3) participants with extreme dietary intake. All participants included in the study provided written informed consent, and fingerprinting was used if participants were unable to write.

The study was approved by the Medical Research Ethics Committee of the Second Affiliated Hospital of Fujian Medical University and Fuwai Cardiovascular Disease Hospital, Beijing, China (No 2020 - 1360). The survey was conducted in accordance with the ethical principles of the Declaration of Helsinki and the International Conference on the Harmonization of Good Clinical Practice.

Definition of hyperuricemia

The normal range of serum uric acid levels is 210–420 μmol/L in adult males and 150–357 μmol/L in adult females, with women's blood uric acid levels approaching those of men after menopause [34]. Participants with fasting serum uric acid levels ≥ 7.0 mg/dL (420 μmol/L) in men and ≥ 6.0 mg/dL (357 μmol/L) in women were defined as hyperuricemic patients [34].

Data collection

Participants completed a standardized questionnaire developed by the National Coordinating Center of Fu Wai Hospital (Beijing, China) through face-to-face interviews with trained staff [35]. The questionnaire included sociodemographic factors (gender, age, occupation, education, marital status, place of residence, economic status, health insurance, etc.), behavioral factors (smoking, alcohol consumption, physical activity, regular sleep,

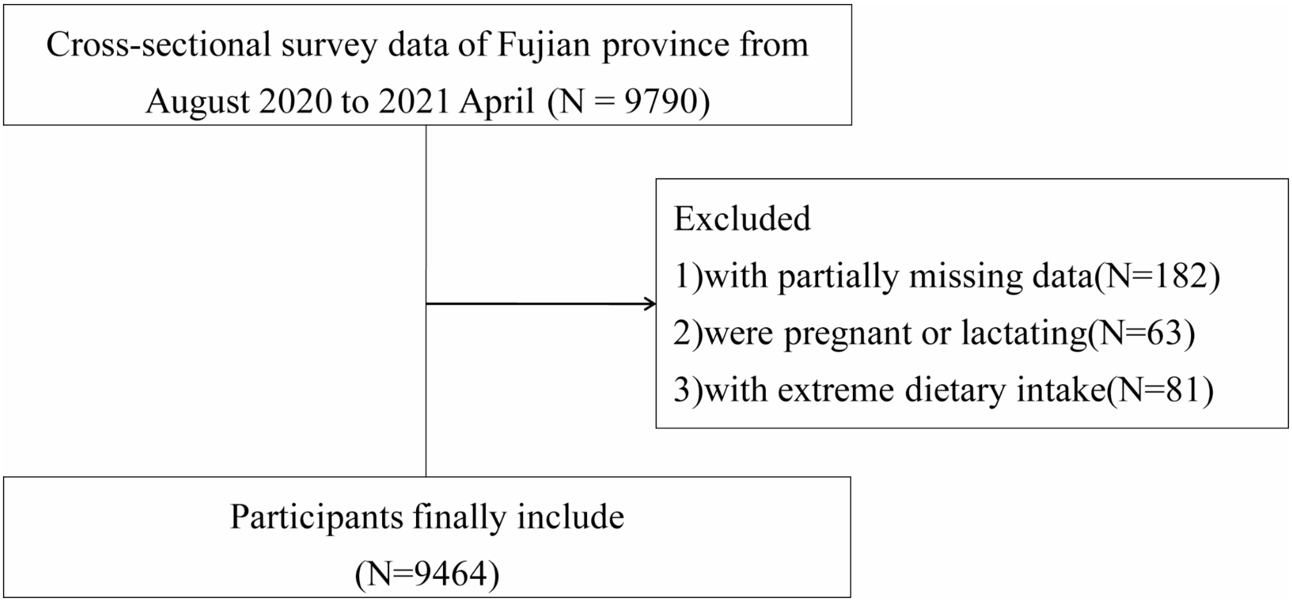

Fig. 1 Flow diagram of study subjects included in the analysis

Table 1 Definition of indicators of oxidative balance score

OBS components	Assignment scheme*
Dietary components	
Consumption of vegetables(A)	0 = low, 1 = intermediate, 2 = high
Consumption of fruits(A)	0 = low, 1 = intermediate, 2 = high
Consumption of fish and other aquatic products(A)	0 = low, 1 = intermediate, 2 = high
Consumption of meat and meat products(P)	0 = high, 1 = intermediate, 2 = low
Lifestyle components	
Tea consumption status(A)	0 = never, 1 = occasional (< 1 day/week), 2 = frequent (≥ 1 day/week)
Physical activity(A)	0 = low (moderate or vigorous activity less than once per week), 1 = moderate (vigorous activity once a week plus moderate activity once a week, or moderate activity 2–4 times a week), 2 = high (vigorous activity twice a week or moderate activity more than 4 times a week)
Smoking status(P)	0 = regular (≥ 1 day/week), 1 = occasional (< 1 day/week), 2 = never
Drinking status(P)	0 = frequent (≥ 1 day/week), 1 = occasional (< 1 day/week), 2 = never
Overweight/obese(P)	0 = obese, 1 = overweight, 2 = normal weight
Abdominal obesity(P)	0 = abdominal obesity, 1 = normal

Low, intermediate, and high categories correspond to tertile values among participants at the baseline survey. P, pro-oxidant; A, anti-oxidant

etc.), personal medical history (hypertension, diabetes, dyslipidemia, hyperuricemia), and family history of hypertension. The physical examination includes measurement of height, weight, body fat, waist circumference, blood pressure, etc.

Assessment of oxidative balance score

As shown in Table 1, a total of 10 food and lifestyle OBS (FoodL-OBS) components were included in this study, including 5 pro-oxidants (meat and meat products, smoking status, alcohol consumption status, obesity and abdominal obesity) and 5 anti-oxidants (vegetables, fruits, fish and other aquatic products, tea consumption status and physical activity). Scores for each component were defined as 0, 1, or 2, except for the abdominal obesity, which was defined as 0 or 1.

Body measurement and assessment of other covariates

Body mass index (BMI) is defined by the following equation: BMI = weight/height^2 (kg/m^2). Overweight was defined as BMI in the range of 24–28 kg/m^2, and obesity was defined as BMI ≥ 28 kg/m^2 [36]. Abdominal obesity was defined as a waist circumference of ≥ 85 cm in men and ≥ 80 cm in women [36].

Blood pressure was measured with the OMRON HBP-1300 Professional Portable Blood Pressure Monitor (OMRON, Kyoto, Japan) by health professionals. According to 2018 Chinese guidelines for the management of Hypertension, hypertension is defined as a systolic blood pressure ≥ 140 mmHg, or a diastolic blood pressure ≤ 90 mmHg, or being on antihypertensive medication [37]. Participants with one or more of the following abnormalities were diagnosed with dyslipidemia: total cholesterol ≥ 6.2 mmol/L, total triglyceride > 2.25 mmol/L, low-density lipoprotein cholesterol > 4.13 mmol/L or high-density lipoprotein cholesterol < 1.03 mmol/L [38]. Diabetes was diagnosed as follows: fasting plasma glucose ≥ 7.0 mmol/L or 2-h postprandial glucose ≥ 11.1

mmol/L [39], or self-reported doctor-diagnosed diabetes or taking diabetes medication.

Statistical analysis

Participants were divided into 4 groups based on quartiles of male and female OBS, respectively. Independent Students t-test was used for comparisons of continuous variables between two groups, and ANOVA was used for comparisons of continuous variables among multiple groups. Chi-Square test was used for comparisons of nominal variables among groups. Univariate and multivariable logistic regression analysis were used to evaluate the association between OBS and hyperuricemia. Subgroup analysis was also performed to examine relationship of OBS with hyperuricemia by the following subgroups: gender (male or female), age (<60 years or ≥60 years), education levels (less than high school, high school, or more than high school), presence of diabetes (yes or no), presence of dyslipidemia (yes or no), and presence of hypertension (yes or no). In order to evaluate dose-response association between continuous OBS and hyperuricemia, a logistic model with restricted cubic spline was used, adjusting for age, gender, education level, household income, presence of hypertension, diabetes, and dyslipidemia.

Statistical analyses were performed using SPSS version 19.0.0.1 (IBM SPSS, 2010, Chicago, IL, USA) and R version 4.3.2 (R Statistical Computing Project). All *P* values were two-tailed and *P* values < 0.05 were considered statistically significant.

Table 2 Baseline characteristics of all participants with hyperuricemia

Variables	Overall (*n* = 9464)	Non- hyperuricemia (*n* = 6745)	hyperuricemia (*n* = 2719)	*P*-Value
Age (years)	44.66 ± 18.06	44.98 ± 17.52	43.87 ± 19.31	0.007
Gender, n (%)				< 0.001
Female	4776(50.46)	3807(79.71)	969(20.29)	
Male	4688(49.54)	2938(62.67)	1750(37.33)	
Age group, n (%)				0.164
< 60 years	7449(78.71)	5334(71.61)	2115(28.39)	
≥ 60 years	2015(21.29)	1411(70.02)	604(29.98)	
Education, n (%)				< 0.001
Less than high school	5041(53.27)	3687(73.14)	1354(26.86)	
High school	1755(18.54)	1194(68.03)	561(21.97)	
More than high school	2668(28.19)	1864(69.87)	804(20.13)	
Hypertension, n(%)				< 0.001
yes	3233(34.16)	1125(34.80)	2108(65.20)	
no	6231(65.84)	4637(74.42)	1594(25.58)	
Diabetes, n(%)				0.943
yes	346(3.66)	100(28.90)	246(71.10)	
no	9118(96.34)	6499(71.28)	2619(28.72)	
Dyslipidemia, n(%)				< 0.001
yes	281(2.97)	173(61.57)	108(38.43)	
no	9183(97.03)	6572(71.57)	2611(28.43)	
Other cardiovascular diseases, n (%)				0.039
yes	109(1.15)	68(62.39)	41(37.61)	
no	9355(98.85)	6677(71.37)	2678(28.63)	
Household income, n (%)				< 0.001
<20 thousand yuan/year	3206(33.88)	2346(73.18)	860(26.82)	
20–50 thousand yuan/year	3996(42.22)	2846(71.22)	1150(28.78)	
>50 thousand yuan/year	2262(23.90)	1553(68.66)	709(31.34)	
OBS	11.33 ± 2.32	11.48 ± 2.29	10.96 ± 2.36	< 0.001
Dietary OBS	3.85 ± 1.57	3.84 ± 1.55	3.86 ± 1.59	0.459
Lifestyle OBS	6.89 ± 1.50	6.99 ± 1.46	6.63 ± 1.56	< 0.001

*P value for the comparison of baseline characteristics of hyperuricemia versus non-hyperuricemia in baseline surveys. Significance was set at $P < 0.05$. OBS, oxidative balance score

Results

Baseline characteristics

A total of 9464 participants from 9790 eligible participants were included in the statistical analysis. Of the 9464 participants, 2719 (28.73%) had hyperuricemia. The prevalence of hyperuricemia was higher in males (1750, 37.33%) than in females (969, 20.29%). Participants with hyperuricemia were younger and less educated (Table 2). Comparison of baseline characteristics showed higher prevalence of hypertension, diabetes mellitus, dyslipidemia and other cardiovascular diseases among hyperuricemic participants. Total OBS, dietary and lifestyle OBS were significantly higher in non-hyperuricemic participants compared to hyperuricemic participants.

Table 3 summarizes the baseline characteristics of the FoodL-OBS quartile array study population. In men, participants in the highest FoodL-OBS quartile were more likely to have lower prevalence of hyperuricemia and hypertension compared with participants in the lowest FoodL-OBS quartil. Compared with participants in the lowest FoodL-OBS quartile, those in the highest FoodL-OBS quartile were more likely to be younger and to have lower prevalence of hyperuricemia, hypertension, diabetes, and dyslipidemia in women. In terms of socioeconomic status, participants in the higher quartiles of the FoodL-OBS were more likely to have higher levels of education and income in both men and women. Table 4 shows the clinical characteristics of each of the FoodL-OBS indicators in men and women. Consistent results in males and females, mean values for vegetables,

Table 3 Baseline characteristics of participants by quartiles of oxidative balance scores for men and women

Characteristics	Oxidative Balance Score									
	Men					Women				
	Quartile 1 (< 9)	Quartile 2 (9–10)	Quartile 3 (11–13)	Quartile 4 (> 13)	P-value	Quartile 1 (< 10)	Quartile 2 (10–11)	Quartile 3 (12–13)	Quartile 4 (> 13)	P-value
Age(years)	44.24 ± 18.12	44.29 ± 18.13	43.86 ± 18.12	45.92 ± 19.41	0.105	50.70 ± 19.53	45.25 ± 18.48	43.45 ± 17.06	43.09 ± 15.84	< 0.001
Hyperuricemia, n(%)					0.003					< 0.001
yes	324(41.81)	474(39.17)	738(35.60)	214(33.97)		205(27.97)	293(21.25)	292(18.32)	179(16.73)	
no	451(58.19)	736(60.83)	1335(64.40)	416(66.03)		528(72.03)	1086(78.75)	1302(81.68)	891(83.27)	
Hypertension, n(%)					< 0.001					< 0.001
yes	392(50.58)	502(41.49)	772(37.24)	189(30.00)		352(48.02)	427(30.96)	383(24.03)	216(20.19)	
no	383(49.42)	708(58.51)	1301(62.76)	441(70.00)		381(51.98)	952(69.04)	1211(75.97)	854(79.81)	
Diabetes, n(%)					0.316					< 0.001
yes	27(3.48)	37(3.06)	78(3.76)	30(4.76)		57(7.78)	55(3.99)	42(2.63)	20(1.87)	
no	748(96.52)	1173(96.94)	1995(96.24)	600(95.24)		676(92.22)	1324(96.01)	1552(97.37)	1050(98.13)	0.026
Dyslipidemia, n(%)					0.879					
yes	27(3.48)	43(3.55)	64(3.09)	22(3.49)		31(4.23)	35(2.54)	36(2.26)	23(2.15)	
no	748(96.52)	1167(96.45)	2009(96.91)	608(96.51)		702(95.77)	1344(97.46)	1558(97.74)	1047(97.85)	
Education level, n (%)					< 0.001					< 0.001
Less than high school	424(54.71)	643(53.14)	986(47.56)	281(44.60)		492(67.12)	784(56.85)	871(54.64)	560(52.34)	
High school	173(22.32)	238(19.67)	505(24.36)	168(26.67)		80(10.91)	184(13.34)	224(14.05)	183(17.10)	
More than high school	178(22.97)	329(27.19)	582(28.08)	181(28.73)		161(21.96)	411(29.80)	499(31.30)	327(30.56)	
Household income, thousand yuan/year, n (%)					0.018					< 0.001
<20	250(32.26)	433(35.79)	660(31.84)	174(27.62)		343(46.79)	502(36.40)	536(33.63)	308(28.79)	
20–50	316(40.77)	477(39.42)	894(43.13)	289(45.87)		276(37.65)	593(43.00)	686(43.04)	465(43.46)	
>50	209(26.97)	300(24.79)	519(25.04)	167(26.51)		114(15.55)	284(20.59)	372(23.34)	297(27.76)	

*P value for the comparison of the baseline characteristics among quartile groups of oxidative balance score at the baseline survey. Significance was set at $P < 0.05$

fruits, meat, fish, and other aquatic products increased with increasing FoodL-OBS quartiles. Significantly higher proportions of participants in the lowest quartile of the FoodL-OBS were regular smokers, regular drinkers, never drinkers of tea, obese, abdominally obese, and physically inactive compared to participants in the highest quartile of the FoodL-OBS.

Relationship between oxidative balance score and hyperuricemia

Table 5 shows the relationship between FoodL-OBS and hyperuricemia. We found an inverse association between FoodL-OBS and hyperuricemia in both men and women. Multivariate logistic regression analyses showed that each additional unit of FoodL-OBS was associated with a 4% and 7% reduction in the risk of hyperuricemia in men [OR: 0.96(0.94,0.99), $P < 0.001$] and women [OR: 0.93(0.90,0.96), $P < 0.001$], respectively. Sensitivity analyses were performed after changing FoodL-OBS from a continuous to a categorical variable. In the fully adjusted model, participants in the highest quartile had a 22% and 37% lower risk of hypertension compared with the lowest quartile of FoodL-OBS in men [0.78(0.62,0.97), $P < 0.001$] and women [OR: 0.63(0.49,0.79), $P < 0.001$], respectively.

Subgroup analyses

Researchers conducted subgroup analyses and interaction tests by age, gender, education, hypertension, diabetes, and dyslipidemia to assess whether the relationship between FoodL-OBS and hyperuricemia was consistent in the general population. The results showed that the inverse association between FoodL-OBS and hyperuricemia remained in all subgroups. As shown in Fig. 2, there were significant interactions between FoodL-OBS and gender, hypertension and dyslipidemia on hyperuricemia ($P_{\text{interaction}} < 0.05$), except for age, education and diabetes ($P_{\text{interaction}} > 0.05$). The inverse effect of FoodL-OBS on hyperuricemia was stronger in the female population

Table 4 Individual components of the score by oxidative balance scores quartile in men and women

Characteristics	Oxidative Balance Score									
	Men					Women				
	Quartile 1 (< 9)	Quartile 2 (9–10)	Quartile 3 (11–13)	Quartile 4 (> 13)	*P*-value	Quartile 1 (< 10)	Quartile 2 (10–11)	Quartile 3 (12–13)	Quartile 4 (> 13)	*P*-value
Vegetable_weight, g/day	204.14 ± 171.65	245.06 ± 230.19	383.67 ± 446.42	600.09 ± 633.62	< 0.001	206.78 ± 228.60	274.77 ± 335.39	390.24 ± 441.46	568.85 ± 742.59	< 0.001
Fruit_weight, g/day	62.15 ± 176.52	92.95 ± 159.54	192.21 ± 320.06	336.50 ± 387.01	< 0.001	61.06 ± 116.48	116.55 ± 208.26	220.90 ± 332.22	363.57 ± 486.83	< 0.001
Meat_weight, g/day	192.58 ± 246.43	172.32 ± 209.40	213.06 ± 313.91	240.70 ± 360.38	< 0.001	186.70 ± 243.56	181.98 ± 268.19	207.75 ± 310.86	206.74 ± 314.17	< 0.001
Fish_weight, g/day	47.10 ± 146.02	54.38 ± 116.23	111.67 ± 225.07	188.70 ± 281.37	< 0.001	38.61 ± 137.12	62.14 ± 140.73	113.98 ± 238.48	175.38 ± 269.51	< 0.001
Obesity status, n (%)					< 0.001	38.61 ± 137.12	62.14 ± 140.73	113.98 ± 238.48	175.38 ± 269.51	< 0.001
Obese	280(36.13)	204(16.86)	159(7.67)	9(1.43)		218(29.74)	166(12.04)	76(4.77)	16(1.50)	
Overweight	336(43.35)	517(42.73)	649(31.31)	131(20.79)		301(41.06)	468(33.94)	392(24.59)	162(15.14)	
Normal weight	159(20.52)	489(40.41)	1265(61.02)	490(77.78)		214(29.20)	745(54.02)	1126(70.64)	892(83.36)	
Abdominal obesity, n (%)					< 0.001					< 0.001
yes	590(76.13)	642(53.06)	737(35.55)	110(17.46)		526(71.76)	625(45.32)	421(26.41)	140(13.08)	
no	185(23.87)	568(46.94)	1336(64.45)	520(82.54)		207(28.24)	754(54.68)	1173(73.59)	930(86.92)	
Smoking status, n (%)					< 0.001					< 0.001
Regular smoker	451(58.19)	553(45.70)	665(32.08)	103(16.35)		20(2.73)	14(1.02)	6(0.38)	1(0.09)	
Occasional smoker	53(6.84)	80(6.61)	156(7.53)	21(3.33)		7(0.95)	16(1.16)	14(0.88)	5(0.47)	
Never smoker	271(34.97)	577(47.69)	1252(60.40)	506(80.32)		706(96.32)	1349(97.82)	1574(98.75)	1064(99.44)	
Drinking status, n (%)					< 0.001					< 0.001
Regular drinker	76(9.81)	61(5.04)	52(2.51)	3(0.48)		52(7.09)	49(3.55)	23(1.44)	7(0.65)	
Occasional drinker	322(41.55)	343(28.35)	492(23.73)	89(14.13)		347(47.34)	468(33.94)	485(30.43)	201(18.79)	
Non-drinker	377(48.65)	806(66.61)	1529(73.76)	538(85.40)		334(45.57)	862(62.51)	1086(68.13)	862(80.56)	
Tea status, n (%)					< 0.001					< 0.001
Non-tea drinkers	386(49.81)	469(38.76)	611(29.47)	121(19.21)		588(80.22)	973(70.56)	873(54.77)	391(36.54)	
Occasional tea drinker	208(26.84)	373(30.83)	632(30.49)	169(26.83)		105(14.32)	284(20.59)	464(29.11)	369(34.49)	
Regular tea drinkers	181(23.35)	368(30.41)	830(40.04)	340(53.97)		40(5.46)	122(8.85)	257(16.12)	310(28.97)	
Physical activity, n (%)					< 0.001					< 0.001
Low (0-1d/wk)	291(37.55)	245(20.25)	188(9.07)	20(3.17)		193(26.33)	211(15.30)	119(7.47)	29(2.71)	
Moderate (2-4d/wk)	273(35.23)	422(34.88)	686(33.09)	163(25.87)		247(33.70)	427(30.96)	440(27.60)	178(16.64)	
High (5-7d/wk)	211(27.23)	543(44.88)	1199(57.84)	447(70.95)		293(39.97)	741(53.73)	1035(64.93)	863(80.65)	

$^*P$ value for the comparison of the baseline characteristics among quartile groups of oxidative balance score at the baseline survey. Significance was set at $P < 0.05$

Table 5 Association between oxidative balance score and hyperuricemia in men and women

Exposure	Men			Women	
	Model 1 [OR(95% CI)]	**Model 2 [OR(95% CI)]**	**Model 3 [OR(95% CI)]**	**Model 1 [OR(95% CI)]**	**Model 3 [OR(95% CI)]**
Oxidative Balance Score (continuous)	0.96(0.93,0.98)	0.96(0.93,0.98)	0.96(0.94,0.99)	0.90(0.87,0.93)	0.93(0.90,0.96)
Oxidative Balance Score (quartile)					
Quartile 1	reference	reference	reference	reference	reference
Quartile 2	0.90(0.75,1.08)	0.92(0.76,1.10)	0.93(0.77,1.12)	0.69(0.57,0.85)	0.78(0.63,0.96)
Quartile 3	0.77(0.65,0.91)	0.77(0.65,0.91)	0.80(0.67,0.95)	0.58(0.47,0.71)	0.68(0.55,0.84)
Quartile 4	0.72(0.58,0.89)	0.71(0.57,0.89)	0.78(0.62,0.97)	0.52(0.41,0.65)	0.63(0.49,0.79)
P for trend	0.003	0.002	0.022	< 0.001	< 0.001

Model 1: No covariates were adjusted. Model 2: Hypertension, education level and household income were adjusted. Model 2: Age, hypertension, diabetes, dyslipidemia, education level and household income were adjusted

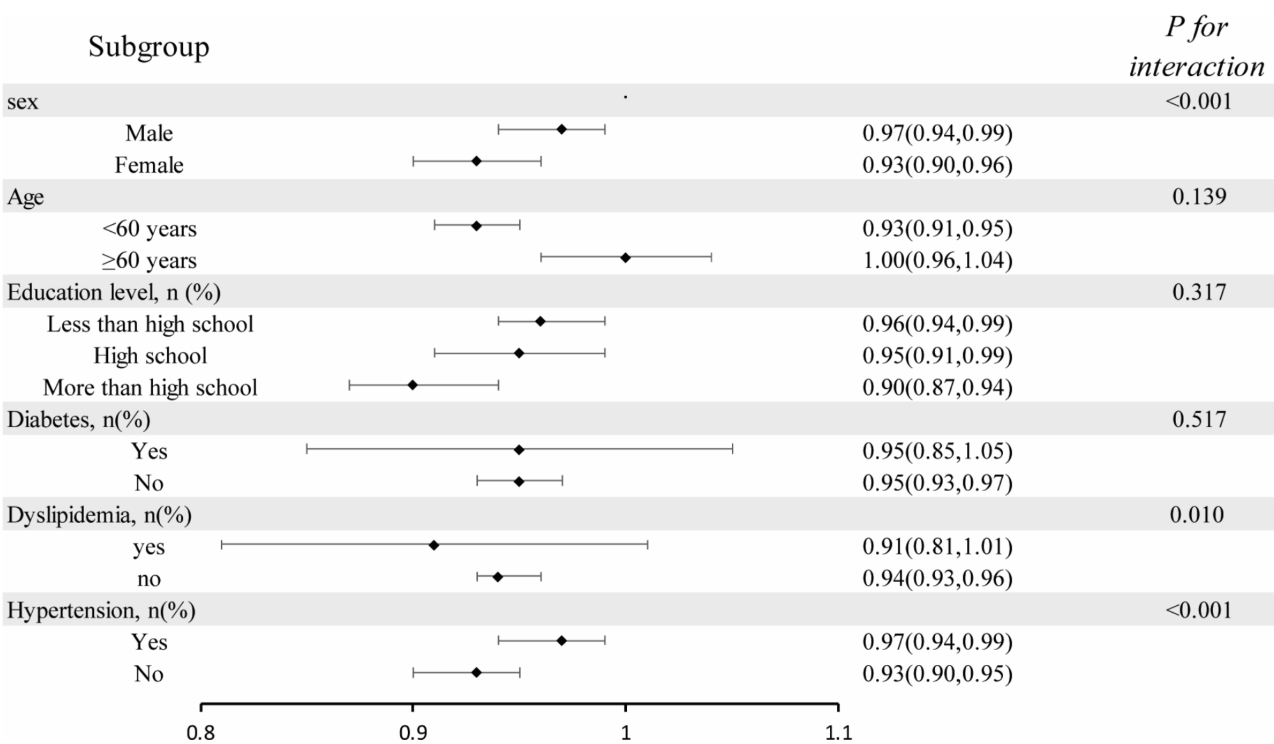

Fig. 2 Subgroup analysis of the association between oxidative balance score and hyperuricemia. Age, sex, education level, hypertension, diabetes and dyslipidemia were adjusted. OR, odds ratio; CI, confidence interval

[0.93(0.90,0.96)] and in the dyslipidemia population [0.91(0.81,1.01)]. In addition, the inverse correlation effect was significantly higher in those without hypertension [0.93(0.90,0.95)] than in those with hypertension [0.97(0.94,0.99)].

RCS analysis

The dose-response relationship between FoodL-OBS and risk of hyperuricemia was further evaluated using RCS curves. As shown in Fig. 3A, the risk of hyperuricemia decreased with increasing FoodL-OBS ($P_{\text{for total}}$<0.001). The relationship between FoodL-OBS and the risk of hyperuricemia was linearly ($P_{\text{nonlinear}}$ = 0.7854). The results of the RCS analysis by gender showed that, consistent with the relationship between overall FoodL-OBS and the risk of hyperuricemia, FoodL-OBS was inversely and linearly associated with the prevalence of hyperuricemia in men ($P_{\text{nonlinear}}$ = 0.9480) and in women ($P_{\text{nonlinear}}$ = 0.1988) (Fig. 3B). And the risk of hyperuricemia decreased with increasing FoodL-OBS, and the reduction in hyperuricemia risk was more pronounced in women than in men. This is also consistent with the results of the subgroup analysis.

Discussion

To the best of our knowledge, this is the first large population based cross-sectional study that explores the association between FoodL-OBS and the risk of hyperuricemia in China. In this cross-sectional study, an inverse association between FoodL-OBS and the risk of

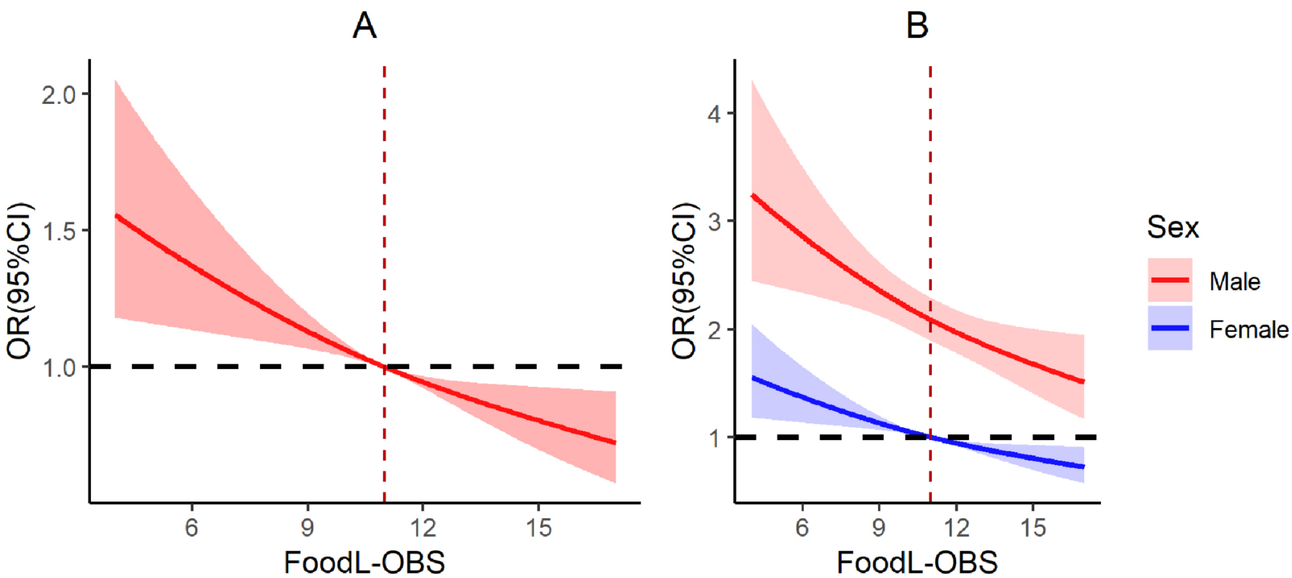

Fig. 3 RCS analysis of the association between FoodL-OBS and hyperuricemia. The association was adjusted for age, gender, education level, household income, hypertension, diabetes, and dyslipidemia. (**A**) RCS curve of the association between FoodL-OBS and hyperuricemia among all participants. (**B**) RCS curve of the association between FoodL-OBS and hyperuricemia among female and male participants. RCS, restricted cubic spline; OR, odds ratio; CI, confidence interval

hyperuricemia was found in both men and women. This association was remained when adjusted for significant covariates. Significant interactions between FoodL-OBS and gender, hypertension and dyslipidemia on hyperuricemia were also found. The inverse effect of FoodL-OBS on hyperuricemia was stronger in women, dyslipidemia, and hypertension participants. Additionally, FoodL-OBS was inversely and linearly associated with the risk of hyperuricemia. The risk of hyperuricemia decreased with increasing FoodL-OBS and was more markedly reduced in women than in men.

Significant association between OBS and hyperuricemia was observed in a few studies [31–33]. In accordance with previous studies, present study demonstrate that high FoodL-OBS could decrease the risk of hyperuricemia. FoodL-OBS represents the overall burden of oxidative stress, which can cause cell and tissue damage, leading to inflammation, cellular damage and various diseases [24–26]. Wang et, al. [31] suggested an inverse association of OBS with hyperuricemia and goat using a population database from the NHANES from 2007 to 2018. Adults with OBS in the second (OR: 0.85, 95% CI: 0.72–0.99), third (OR: 0.71, 95% CI: 0.58–0.85), and fourth (OR: 0.48, 95% CI: 0.38–0.61) quartiles had a reduced risk of hyperuricaemia compared with adults with OBS in the first quartile. Another study including participants in the NHANES from 2007 to 2018 underscored a robust inverse association of OBS with serum uric acid levels and the incidence of hyperuricemia [32]. The OR (95% CI) was 0.80 (0.67 to 0.97) for the third quartile of OBS and 0.55 (0.44 to 0.70) for the fourth quartile of OBS compared with the reference category for the first quartile of OBS. Using the NHANES database from 2011 to 2018, Yang et, al. [33] found that serum uric acid levels and prevalence of hyperuricemia in US adults exhibited an inverse association with OBS. Compared to Quartile 1, participants in Quartile 4 had a 38% lower prevalence of hyperuricemia [0.62 (0.55, 0.71)]. Similar to the risk estimates from these studies, in the present study, participants in the highest quartile had a 22% and a 37% lower risk of hypertension compared with the lowest quartile of FoodL-OBS in men [0.78(0.62,0.97)] and women [OR: 0.63(0.49,0.79)], respectively.

There are some possible mechanisms by which OBS is related to hyperuricemia. High activity of xanthine oxidase is a contributing factor to hyperuricemia, which leads to excessive production of uric acid, which is concentrated in the extremities [40]. Xanthine oxidoreductase is a rate-limiting enzyme in purine catabolism, which catalyzes the oxidation of hypoxanthine to xanthine and xanthine to uric acid, and produces reactive oxygen species (ROS) [22]. Yang et, al. [41] found that inhibition of xanthine oxidase protects against diabetic kidney disease through the amelioration of oxidative stress. Oxidative stress is a condition in which the cell's antioxidant clearance system is overwhelmed by the overproduction of ROS, resulting in the oxygen paradox [42]. Previous study indicated that Uric acid promotes the production of ROS and activates several inflammatory signaling pathways, and then lead to higher oxidative stress level [43]. Liu et, al. [22] showed that oxidative stress played an important role in the development of hyperuricemia at a certain level.

Subgroup analysis and interaction test revealed that the risk of hyperuricemia decreased with increasing FoodL-OBS, and the reduction in hyperuricemia risk was more pronounced in women, dyslipidemia and non-hypertension populations. In consistent with our results, several studies indicated that women were at lower level of uric acid and lower risk of hyperuricemia [44–47]. This perhaps related to a regulation of sex hormones levels, which were reported to be independently associated with hyperuricemia and were contributed to the development of obesity [45, 48]. The prevalence of hyperuricemia was observed to decrease with the increase of OBS in various subgroups of hypertension and dyslipidemia. Metabolic disorders, including hyperuricemia, hypertension, and dyslipidemia are closely linked with insulin resistance [49]. And the pathological and physiological pathogenesis mechanism of insulin resistance may be oxidative stress and inflammation [50].

This study has several strengths of note. First, this is the first large population-based cross-sectional study that examines the association between FoodL-OBS and the risk of hyperuricemia in China. Second, the use of whole-population random sampling can include accurate representative samples and eliminate sampling bias. Last, the OBS assessment in this study was calculated based on 10 food and lifestyle components, which are simpler and easier to use. There are still some shortcomings in present study. Firstly, this is a cross-sectional study, and the casual inference was not allowed. Secondly, for self-reported diet and other data, measurement errors are inevitable. However, in this study standardized face-to-face interviews and physical examination performed by trained staff have minimized the impact of measurement errors. Finally, although a comprehensive set of confounders were considered, it is possible that the presence of confounders was not measured as an observational study. For example, endogenous factors that alter oxidative stress (gut microbiota and genes associated with antioxidant enzymes) and environmental factors (air and water pollutants, UV radiation, pathogen infection, and extreme temperatures). However, we substantiated the effects of FoodL-OBS on hyperuricemia, by multiple statistical methods including subgroup analysis and RCS analysis.

Conclusions

In conclusion, an inverse association as well as dose-response relationship between FoodL-OBS and hyperuricemia were observed. Significant interactions between FoodL-OBS and gender, hypertension and dyslipidemia on hyperuricemia were also detected. The risk of hyperuricemia decreased with increasing FoodL-OBS and was more markedly reduced in women than in men. Maintaining an appropriate body weight, physical activity, a non-smoking, non-alcoholic, as well as regular tea-drinking lifestyle, and a healthy dietary pattern could be effective in reducing the risk of hyperuricemia. And it may be more effective in women than in men. However, large prospective cohort studies and randomized controlled trials are needed to verify the effect of OBS on hyperuricemia and elucidate its causal mechanism.

Abbreviations

OBS	Oxidative balance score
NHANES	National health and nutrition examination survey
FoodL-OBS	Food and lifestyle OBS
BMI	Body mass index
ROS	Reactive oxygen species

Acknowledgements
We would like to express their gratitude to all participants for their cooperation and to all staffs for recruiting subjects and their technical assistance.

Author contributions
Conception and design (PXE and HY), data collection (PHW, HJR, QWX, CHJ, and FJW), data analysis (PHW and HY), data interpretation (PHW, HJR, QWX, and PXE), manuscript drafting and revising (PHW, HY, HJR, QWX, CHJ, FJW, and PXE). All authors have discussed the results and commented on the manuscript. All authors read and approved the final manuscript to be published.

Funding
This work was supported by the Fujian Provincial Finance Project (No. BPBHY2021).

Data availability
The datasets of the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The Medical, Research Ethics Committee of the Second Affiliated Hospital of Fujian medical University and the Fuwai Cardiovascular Hospital of Beijing, China approved the study protocol, which complied with the Declaration of Helsinki (ethics number: 2020 – 1360). All participants provided their informed consent before they participated in this study.

Consent for publication
No data of any individual person's data in any form (including any individual details, images or videos) will be used in this study.

Competing interests
The authors declare no competing interests.

Received: 13 August 2024 / Accepted: 10 January 2025
Published online: 20 January 2025

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