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The Association of Phytochemical Index and oxidative balance score with bone Mineral density: a case-control study

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Abstract

Background Phytochemical index (PI) and oxidative balance score (OBS) have not been previously evaluated in women with osteoporosis. The present study aimed to investigate their relationship with bone mineral density (BMD) in postmenopausal women.

Methods The current case-control study included healthy postmenopausal women ($n=131$) and postmenopausal women with abnormal BMD (osteopenia: T-score between −1 and −2.5; osteoporosis: T-score less than −2.5) ($n=131$). All participants were recruited from the Isfahan Bone Densitometry Center. Dual-energy X-ray absorptiometry (DXA) measured BMD at the lumbar vertebrae and femoral neck, expressed in grams per square centimeter. A validated semi-quantitative food frequency questionnaire was used to assessed PI and OBS. Binary logistic regression was performed to analyze the association between PI and OBS with BMD.

Results A positive association was observed between PI and both lumbar and femoral BMD ($P<0.001$ for both of them). Similarly, a significant positive association was found between OBS and both lumbar and femoral BMD ($P<0.001$ for both of them). Compared to the first tertile of PI, significantly higher odds of abnormal BMD were observed in the last tertile across all models (crude model: odds ratio (OR) = 0.25, 95% confidence interval (CI): 0.13–0.46, $P<0.001$ - adjusted model 1: OR = 0.23, 95% CI: 0.12–0.44, $P<0.001$ - adjusted model 2: OR = 0.28, 95% CI: 0.14–0.55, $P<0.001$). Similarly, compared to the first tertile of OBS, higher odds of abnormal BMD were in the last tertile across all models (crude model: OR = 0.25, 95% CI: 0.13–0.47, $P<0.001$ - adjusted model 1: OR = 0.24, 95% CI: 0.13–0.46, $P<0.001$ - adjusted model 2: OR = 0.26, 95% CI: 0.13–0.52, $P<0.001$).

Conclusions Overall, the present study highlighted the important role of PI and OBS in abnormal BMD. The findings indicated that higher PI and OBS were inversely associated with the odds of abnormal BMD.

Keywords Phytochemical index, Oxidative balance score, Bone density, Osteoporosis

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Introduction

Oxidative stress occurs when there is an imbalance between the excessive production of reactive oxygen species (ROS) and the inadequacy of the antioxidant defense system [1, 2]. Factors such as aging, hormonal changes (e.g., decreased estrogen levels), pathological conditions involving excessive production of inflammatory cytokines, radiation exposure, and certain drug therapies contribute to this imbalance and aggravate oxidative stress [1, 3–5]. Oxidative stress contributes to the pathogenesis of various diseases, including bone disorder, through mechanisms such as lipid peroxidation, structural changes in cell membrane, and oxidation of proteins and nucleic acid [1]. A reduced intake of phytochemicals is another potential factor leading to increased oxidative stress [6]. Regular monitoring of phytochemicals intake could play a significant role in promoting health and preventing disease [6]. Yoo et al. demonstrated a positive link between a higher dietary phytochemical index (DPI) and a lower risk of osteoporosis in postmenopausal women [7]. They further proposed that the highest quartile of DPI was related to a 16% lower risk of osteoporosis compared to the lowest quartile. These findings suggest that diets rich in phytochemicals may have protective effects on bone health [7].

In this context, the dietary phytochemical content can be assessed using an index known as the phytochemical index (PI), which was presented in 2004 [8]. This index is calculated as the percentage of total dietary calories obtained from foods high in phytochemicals, including whole grains, legumes, vegetables (excluding potatoes), fruits, nuts, seeds, and, relative to total caloric intake [9]. PI is a suitable tool for evaluating dietary phytochemical intake and their beneficial effects on health [9]. Phytochemicals encompass polyphenols, alkaloids, terpenoids, flavonoids, saponins, and steroids, which act as physiologically active compounds in a variety of plant-based foods, including whole grains, legumes, vegetables, and fruits [9, 10]. Phytochemicals are bioactive compounds that significantly reduce the risk of chronic diseases. Among their potential protective effects, phytochemical-rich diets are particularly effective in reducing oxidative stress and inflammation [6].

Determining oxidative stress levels and dietary phytochemical intake appears to play a significant role in managing bone disorders [11]. Studies have also highlighted the crucial role of oxidative stress in postmenopausal osteoporosis [12, 13]. The oxidative balance score (OBS) has been proposed as a comprehensive criterion of oxidative balance, integrating information on dietary and lifestyle factors to reflect life stressors [11]. This index is calculated based on an individuals' exposures to antioxidants and pro-oxidants, reflecting their nutrition and lifestyle behaviors [14]. It has been shown that a higher OBS is related to a lower risk of several metabolic disorders [14, 15]. Shahriarpour et al. demonstrated that a higher OBS, which reflects a greater presence of antioxidants compared to pro-oxidant exposures, is associated with a reduced risk of osteoporosis [16]. These finding highlight the important role of an antioxidant-rich diet in protecting against bone density loss [17].

Since the relationship between the PI and OBS with bone mineral density (BMD) in postmenopausal women with osteopenia or osteoporosis has not been already studied, the current research aimed to investigate this association. If such a relationship exists, adopting a comprehensive approach involving lifestyle and dietary modification may help reduce oxidative stress in the pathways contributing to the pathogenesis of osteoporosis or osteopenia, thereby aiding in the prevention or even treatment of these conditions.

Methods

Study population

The current case-control study was conducted on healthy postmenopausal women (without abnormal BMD) ($n = 131$) and postmenopausal women with abnormal BMD ($n = 131$), aged 45–65 years. All participants were recruited from the Isfahan Bone Densitometry Center (Mahdieh), Iran, using a convenient sampling method between May to December 2021. Based on the study by Shivappa et al., considering an odds ratio (OR) of 2.30, $\alpha = 0.05$ and $\beta = 20\%$ [18], the sample size was computed. Menopause was defined as the cessation of menstrual cycles for at least 12 consecutive months. Exclusion criteria included premenopausal women, individuals who consumed glucocorticoids or alcohol, and those with a history of chemotherapy or diseases such as cancer, rheumatoid, renal disease, and diabetes. Also, participants with over-reported (> 4200 kcal/day) or under-reported (< 800 kcal/day) energy intake were excluded. The control group was randomly selected from the same center and included individuals referred for dual-energy X-ray absorptiometry (DXA) for reasons other than osteoprosis.

Using standardized methods, participants' height and body weight were measured. The Body Mass Index (BMI) was calculated by dividing body weight (kg) by the square of their height (m^2). A general checklist was used to collect participant's basic characteristics, including socio-demographic information, contextual factors, and confounding variables like weight, BMI, the use of medication and supplements, and socioeconomic status that may influence BMD. Physical activity levels were assessed using the International Physical Activity Questionnaire (IPAQ). Based on the guidelines, physical activity was categorized into three levels: high activity (above 3000 metabolic equivalents of task (MET)-minutes/week),

moderate activity (between 600 and 3000 MET-minutes/week), and low activity (below 600 MET-minutes/week) [19].

BMD measurement

To diagnose osteoporosis or osteopenia in women, DXA (device model: Horizon Wi (S/N 200451)) was used to measure BMD at the lumbar vertebrae and femoral neck [20]. According to World Health Organization (WHO) criteria, a T-score of less than − 2.5 indicated osteoporosis, a T-score between − 1 and − 2.5 indicated osteopenia, and a T-score greater than − 1 was considered normal bone mass. The case group included individuals diagnosed with osteoporosis or osteopenia, while the control group included those with normal bone mass.

Dietary assessment and food grouping

To evaluate participant's dietary intake over the past year, a validated semi-quantitative food frequency questionnaire (FFQ) was applied [21]. The dietary PI was determined by the McCarty et al. method [22], according to the following formula: [PI = (daily energy extracted by foods high in phytochemicals (kcal) / total daily energy intake (kcal)) × 100]. Foods considered high in phytochemicals included olive oil, seeds, soy products, nuts, whole grains, legumes, vegetables, and fruits. Vegetable juices, natural fruit, and tomato sauces, were also recognized for their elevated phytochemical content and incorporated into the calculations. Therefore, these foods were considered in calculations. A higher consumption of these foods corresponded to a higher total PI score [22, 23].

The OBS was calculated based on pro- and antioxidant contributors derived from the FFQ to assess oxidative balance. The dietary components representing pro-oxidants included saturated fatty acids (SFA), polyunsaturated fatty acids (PUFA), and iron, while antioxidants included fiber, lycopene, lutein, β-carotene, α-carotene, vitamin E, vitamin C, B_9, zinc, and selenium. The antioxidant values were classified into tertiles, scoring between 0 and 2 points. In contrast, pro-oxidants were scored in reverse, with the highest tertile receiving 0 points and the lowest tertile receiving two points (Table 1) [23, 24].

Ethical statement

The research procedures and protocols received approval from the Ethical Committee of Tabriz University of Medical Sciences (Ethical Approval Code: IR.TBZMED.REC.1400.114, Pazhoohan Code: 66934), and all participants provided informed consent. Some detail of the present study has been previously published [25–27].

Statistical analysis

The SPSS (version 26.0) was applied to analyze the data. A p-value of less than 0.05 was considered statistically significant. Individuals were classified into tertiles of PI

Table 1 Oxidative balance score components

OBS components	Assignment scheme
Non-dietary pro-oxidants	
Obesity	0 = BMI ≥ 30 kg/m^2 AND WC ≥ 0.88 m in females 1 = BMI ≥ 30 kg/m^2 OR WC ≥ 0.88 m in females 2 = BMI < 30 kg/m^2 AND WC < 0.88 m in females m
Smoking	0 = current, 1 = former and 2 = never
Non-dietary antioxidants	
Physical activity (MET-min/d)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Dietary pro-oxidants	
SFA (g)	0 = high (3rd tertile), 1 = medium (2nd tertile), and 2 = low (1st tertile)
PUFA (g)	0 = high (3rd tertile), 1 = medium (2nd tertile), and 2 = low (1st tertile)
Iron (mg)	0 = high (3rd tertile), 1 = medium (2nd tertile), and 2 = low (1st tertile)
Dietary antioxidants	
Fiber (g)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Vitamin E (mg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Vitamin C (mg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Vitamin B_9 (μg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Alpha-carotene (μg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Beta-carotene (μg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Lutein (μg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Lycopene (μg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Zinc (mg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)
Selenium (μg)	0 = low (1st tertile), 1 = medium (2nd tertile), and 2 = high (last tertile)

OBS, oxidative balance score; BMI, body mass index; WC, waist circumference; MET, metabolic equivalent of task; SFA, saturated fatty acid; PUFA, poly-unsaturated fatty acid

and OBS. The Kolmogorov-Smirnov test was used to assess the normality of the data distribution. Baseline features were reported as frequencies (percentages) for categorical variables and medians (interquartile ranges (IQR)) or means ± standard deviations (SD) for continuous variables, using the chi-squared test, Mann-Whitney, and independent sample T-test, respectively. One-way analysis of variance (ANOVA), followed by Tukey's test, was performed to analyze the nutrient and food groups. The correlation between femoral and lumbar BMD with PI and OBS was assessed using Pearson's correlation. Binary logistic regression was utilized to examine the relationship between PI and OBS and BMD abnormalities in both continues and categorical conditions. Age and BMI were adjusted for in the first model, while education, physical activity, income, vitamin D, and calcium supplements were additionally adjusted for in the second model. R language (version 4.4.1) was used, along with the "ggplot2" and "gridExtra" packages, for creating bar plots.

Results

The baseline features of the study participants are shown in Table 2. The results indicated that the mean age in the control group was significantly lower than that in the case group ($P = 0.036$). However, femoral and lumbar BMD, as well as the total PI and OBS scores, were significantly greater in the control group ($P < 0.001$ for both). Furthermore, vitamin D supplementation ($P = 0.018$), education level ($P < 0.001$), and physical activity ($P = 0.010$) differed significantly between the case and control groups.

Table 2 Baseline characteristics of study participants

Variables	Case ($n = 131$)	Control ($n = 131$)	*P*-value
Age (year)[1]	57.95 ± 5.42	56.47 ± 5.91	**0.036**
BMI (kg/m^2)[1]	29.78 ± 3.99	29.13 ± 3.31	0.150
BMD femoral (g/cm^2)[1]	0.64 ± 0.09	0.78 ± 0.07	**<0.001**
BMD lumbar (g/cm^2)[1]	0.81 ± 0.09	1.00 ± 0.08	**<0.001**
Total PI (energy %)[2]	22.55 (14.62)	29.15 (17.74)	**<0.001**
Total OBS score[2]	15.0 (6.0)	19.0 (9.0)	**<0.001**
Income, high (%)[3]	66 (50.4)	78 (59.5)	0.086
Physical activity, moderate (%)[3]	9 (6.9)	22 (16.8)	**0.010**
Education level (%)[3]			**<0.001**
Under diploma	98 (74.8)	65 (49.6)	
Diploma	25 (19.1)	52 (39.7)	
Higher diploma	8 (6.1)	14 (10.7)	
Calcium supplement, yes (%)[3]	32 (24.4)	32 (24.4)	1.000
Vitamin D supplement, yes (%)[3]	58 (44.3)	76 (58.0)	**0.018**

Abbreviations: BMI, body mass index; kg, kilogram; m, meter; g, gram; cm, centimeter; PI, phytochemical index; OBS, oxidative balance score

[1] Using independent samples T-test for parametric continuous variables and values are mean ± SD

[2] Using Mann-Whitney for non-parametric continuous variables and values are median (IQR)

[3] Using chi-square test for categorical variables and values are number (percentage)

Nutrient and food group intakes across tertiles of PI are reported in Table 3. According to the results, the intake of sodium, oil, and refined grains ($P < 0.001$ for all), as well as vitamin E ($P = 0.032$) was lower in the highest tertile of PI in comparison to the lowest tertile. In contrast, protein, fiber, vitamins A, K, B_6, and C, as well as calcium, magnesium, zinc, copper, fruits, vegetables, nuts, and legumes were higher in the last tertile ($P < 0.001$ for all, except for calcium and zinc).

According to Table 4, the intake of energy, carbohydrates, dairy, legumes, nuts, vegetables, zinc, magnesium, calcium, protein, fat, fiber, SFA, MUFA, PUFA, vitamin C, A, E, K, B_6, B_9, B_{12}, iron, copper, fruits and meats were greater in the highest tertile of OBS ($P < 0.001$ for all, except fat, PUFA, and vitamin E). However, sweets and sugar-sweetened beverages were lower in the last tertile of OBS ($P = 0.013$).

The prevalence of abnormal BMD according to the tertiles of PI and OBS is shown in Figs. 1 and 2. Compared to the first tertile, the prevalence of abnormal BMD was significantly lower in the last tertile of both PI and OBS ($P < 0.001$ for both).

The correlation between femoral and lumbar BMD with PI and OBS is shown in Table 5. A positive relationship was found between PI and both lumbar and femoral BMD ($P < 0.001$ for both). Similarly, a significant positive association was found between the OBS and both lumbar and femoral BMD ($P < 0.001$ for both).

The association between PI and OBS with abnormal BMD is reported in Table 6. Lower odds of abnormal BMD were found with each unit increase in PI (crude model: odds ratio (OR) = 0.96, 95% confidence interval (CI): 0.94–0.98, $P < 0.001$ - adjusted model 2: OR = 0.96, 95% CI: 0.94–0.98, $P = 0.001$). Similarly, lower odds of abnormal BMD were found with each unit change in OBS (crude model: OR = 0.87, 95% CI: 0.83–0.92, $P < 0.001$ - adjusted model 1: OR = 0.87, 95% CI: 0.82–0.92, $P < 0.001$ - adjusted model 2: OR = 0.88, 95% CI: 0.83–0.93, $P < 0.001$).

In comparison to the first tertile of PI, higher and statistically significant odds of abnormal BMD were observed in the last tertile of PI in all models (crude model: OR = 0.25, 95% CI: 0.13–0.46, $P < 0.001$ - adjusted model 1: OR = 0.23, 95% CI: 0.12–0.44, $P < 0.001$ - adjusted model 2: OR = 0.28, 95% CI: 0.14–0.55, $P < 0.001$). Similarly, in comparison to the first tertile of OBS, higher and statistically significant odds of abnormal BMD were found in the last tertile of OBS in all models (crude model: OR = 0.25, 95% CI: 0.13–0.47, $P < 0.001$ - adjusted model 1: OR = 0.24, 95% CI: 0.13–0.46, $P < 0.001$ - adjusted model 2: OR = 0.26, 95% CI: 0.13–0.52, $P < 0.001$).

Table 3 Nutrients and food groups intake between tertiles of phytochemical index

Variables	T_1 ($n=87$)	T_2 ($n=88$)	T_3 ($n=87$)	*P*-value
Nutrients				
Energy (kcal/d)	2095.79 ± 386.67 [a]	2149.20 ± 351.73 [a]	2135.63 ± 339.76 [a]	0.595
Carbohydrates (g/day)	307.11 ± 58.85 [a]	317.94 ± 50.26 [a]	318.18 ± 47.91 [a]	0.285
Protein (g/day)	63.13 ± 12.73 [a]	67.58 ± 12.69 [b]	70.87 ± 12.55 [b]	**< 0.001**
Fat (g/day)	74.60 ± 15.34 [a]	75.30 ± 14.60 [a]	72.54 ± 13.17 [a]	0.421
Fiber (g/day)	27.33 ± 4.20 [a]	31.76 ± 4.54 [b]	34.15 ± 7.02 [c]	**< 0.001**
SFA (g/day)	18.55 ± 5.70 [a]	18.89 ± 4.96 [a]	18.71 ± 3.97 [a]	0.906
MUFA (g/day)	26.58 ± 4.55 [a]	26.81 ± 4.95 [a]	26.81 ± 4.91 [a]	0.927
PUFA (g/day)	19.20 ± 2.98 [a]	19.13 ± 3.36 [a]	18.57 ± 4.49 [a]	0.472
Vitamin A (RAE/day)	344.10 ± 166.19 [a]	485.26 ± 183.60 [b]	625.52 ± 350.04 [c]	**< 0.001**
Vitamin E (mg/day)	22.26 ± 4.43 [a]	22.90 ± 3.57 [a, b]	21.13 ± 5.30 [b]	**0.032**
Vitamin K (mg/day)	92.57 ± 40.63 [a]	131.82 ± 59.51 [b]	165.66 ± 96.90 [c]	**< 0.001**
Vitamin B_6 (mg/day)	1.52 ± 0.29 [a]	1.68 ± 0.29 [b]	1.86 ± 0.39 [c]	**< 0.001**
Vitamin B_9 (µg/day)	454.30 ± 78.27 [a]	466.26 ± 78.92 [a]	471.13 ± 83.97 [a]	0.369
Vitamin B_{12} (µg/day)	2.74 ± 1.78 [a]	2.97 ± 1.34 [a]	2.94 ± 1.06 [a]	0.515
Vitamin C (mg/day)	95.55 ± 43.35 [a]	146.69 ± 54.00 [b]	186.72 ± 76.96 [c]	**< 0.001**
Sodium (mg/day)	3859.01 ± 546.80 [a]	3694.02 ± 518.99 [b]	3502.84 ± 478.74 [b]	**< 0.001**
Calcium (mg/day)	397.65 ± 318.84 [a]	503.60 ± 272.58 [b]	565.73 ± 285.93 [b]	**0.001**
Magnesium (mg/day)	386.08 ± 61.02 [a]	421.51 ± 69.46 [b]	441.56 ± 80.65 [b]	**< 0.001**
Iron (mg/day)	14.72 ± 1.95 [a]	15.30 ± 2.14 [a]	15.47 ± 2.35 [a]	0.055
Zinc (mg/day)	10.27 ± 2.07 [a]	11.18 ± 2.26 [b]	11.59 ± 2.43 [b]	**0.001**
Copper (mg/day)	1.45 ± 0.24 [a]	1.59 ± 0.27 [b]	1.68 ± 0.29 [c]	**< 0.001**
Food groups				
Whole grains (g/day)	220.15 ± 41.85 [a]	212.51 ± 47.85 [a]	206.02 ± 51.37 [a]	0.143
Fruits (g/day)	301.58 ± 139.60 [a]	458.51 ± 143.04 [b]	596.84 ± 204.17 [c]	**< 0.001**
Vegetables (g/day)	158.74 ± 58.89 [a]	245.23 ± 91.27 [b]	305.30 ± 134.52 [c]	**< 0.001**
Nuts (g/day)	4.39 ± 0.43 [a]	11.23 ± 1.09 [b]	14.74 ± 11.84 [b]	**< 0.001**
Legumes (g/day)	21.99 ± 1.16 [a]	27.28 ± 1.38 [b]	30.73 ± 1.92 [b]	**< 0.001**
Oil (g/day)	31.23 ± 4.77 [a]	29.09 ± 6.42 [a]	27.79 ± 6.07 [b]	**< 0.001**
Refined grains (g/day)	267.61 ± 106.40 [a]	237.99 ± 96.09 [b]	202.99 ± 81.46 [b]	**< 0.001**
Dairy (g/day)	217.23 ± 187.94 [a]	253.36 ± 157.16 [a]	270.32 ± 138.56 [a]	0.091
Meat (g/day)	36.65 ± 14.61 [a]	37.15 ± 14.00 [a]	37.02 ± 13.57 [a]	0.472
Sweets & sugar beverages (g/day)	37.02 ± 2.34 [a]	5.87 ± 1.26 [a]	18.94 ± 2.38 [b]	**< 0.001**

Abbreviations: kcal, kilocalorie; g, gram; SFA, saturated fatty acid; PUFA, polyunsaturated fatty acid; MUFA, monounsaturated fatty acid; RAE, retinol activity equivalents; mg, milligram; µg, microgram

Values are presented as mean ± SD

A one-way ANOVA test followed by Tukey's test was used

Welch's One-way ANOVA test followed by Tukey's test was used

Means with the same superscript letters (aa, bb, or cc) are not significantly different ($p > 0.05$)

Discussion

The present study assessed the relationship between PI and OBS with abnormal BMD in postmenopausal women. A higher PI and OBS were directly associated with higher femoral and lumbar BMD. Additionally, the findings revealed lower odds of abnormal BMD with higher PI and OBS.

The results showed that people in the upper tertile of PI had lower odds of abnormal BMD in comparison to those in the first tertile. Several mechanisms explain the relationship between PI and bone health. Oxidative stress occurs when there is an imbalance between the production of ROS and the body's antioxidant defense system, which negatively impacts bone health [28]. Oxidative stress disrupts the balance between osteoclast and osteoblast, leading to chronic metabolic disorders [1]. It has been reported that ROS and antioxidant systems play a crucial role in bone loss [1]. In this context, oxidative stress promotes pre-osteoclast differentiation into osteoclast and enhances bone resorption [1, 29, 30]. On the other hand, increased ROS levels inducing apoptosis of osteocytes, leading to an imbalance in bone remodeling and ultimately impairing bone formation [1].

In this regard, it has been shown ROS are involved in inducing apoptosis of osteocytes and osteoblasts, favoring osteoclastogenesis [1]. Antioxidants, by

Table 4 Nutrients and food groups intake between tertiles of oxidative balance score

Variables	T_1 ($n=82$)	T_2 ($n=89$)	T_3 ($n=91$)	*P*-value
Nutrients				
Energy (kcal/d)	1979.26 ± 318.859 [a]	2092.36 ± 280.58 [b]	2293.89 ± 395.66 [c]	**< 0.001**
Carbohydrates (g/day)	291.67 ± 49.72 [a]	308.51 ± 40.00 [b]	340.71 ± 55.02 [c]	**< 0.001**
Protein (g/day)	58.67 ± 7.65 [a]	66.52 ± 10.83 [b]	75.54 ± 13.64 [c]	**< 0.001**
Fat (g/day)	70.50 ± 12.65 [a]	73.31 ± 12.36 [a]	78.27 ± 16.66 [b]	**0.001**
Fiber (g/day)	26.35 ± 3.54 [a]	30.33 ± 4.13 [b]	36.08 ± 5.73 [c]	**< 0.001**
SFA (g/day)	16.77 ± 3.70 [a]	18.62 ± 4.75 [b]	20.56 ± 5.36 [c]	**< 0.001**
MUFA (g/day)	25.23 ± 2.99 [a]	26.61 ± 4.06 [a]	28.24 ± 6.17 [b]	**< 0.001**
PUFA (g/day)	18.15 ± 2.77 [a]	18.99 ± 3.58 [a, b]	19.68 ± 4.28 [b]	**0.022**
Vitamin A (RAE/day)	294.89 ± 106.42 [a]	434.68 ± 120.91 [b]	705.42 ± 324.49 [c]	**< 0.001**
Vitamin E (mg/day)	21.14 ± 4.04 [a]	21.91 ± 4.40 [a, b]	23.14 ± 4.88 [b]	**0.013**
Vitamin K (mg/day)	84.54 ± 41.35 [a]	114.26 ± 36.51 [b]	186.42 ± 91.49 [c]	**< 0.001**
Vitamin B_6 (mg/day)	1.39 ± 0.14 [a]	1.65 ± 0.24 [b]	2.00 ± 0.34 [c]	**< 0.001**
Vitamin B_9 (µg/day)	424.10 ± 73.05 [a]	451.78 ± 62.99 [b]	511.64 ± 78.64 [c]	**< 0.001**
Vitamin B_{12} (µg/day)	2.28 ± 1.02 [a]	2.95 ± 1.57 [b]	3.37 ± 1.40 [b]	**< 0.001**
Vitamin C (mg/day)	82.91 ± 28.17 [a]	128.03 ± 34.66 [b]	211.79 ± 64.25 [c]	**< 0.001**
Sodium (mg/day)	3731.10 ± 554.36 [a]	3651.18 ± 423.05 [a]	3677.47 ± 609.75 [a]	0.612
Calcium (mg/day)	643.81 ± 164.25 [a]	831.33 ± 264.01 [b]	1022.53 ± 315.90 [c]	**< 0.001**
Magnesium (mg/day)	365.12 ± 47.35 [a]	414.10 ± 63.45 [b]	464.87 ± 72.33 [c]	**< 0.001**
Iron (mg/day)	14.12 ± 1.72 [a]	14.95 ± 1.66 [b]	16.31 ± 2.43 [c]	**< 0.001**
Zinc (mg/day)	9.66 ± 1.67 [a]	10.99 ± 2.18 [b]	12.25 ± 2.27 [c]	**< 0.001**
Copper (mg/day)	1.39 ± 0.19 [a]	1.56 ± 0.25 [b]	1.76 ± 0.27 [c]	**< 0.001**
Food groups				
Whole grains (g/day)	209.50 ± 42.42 [a]	218.90 ± 50.74 [a]	210.08 ± 47.79 [a]	0.337
Fruits (g/day)	277.09 ± 111.80 [a]	419.99 ± 106.36 [b]	641.88 ± 181.04 [c]	**< 0.001**
Vegetables (g/day)	153.36 ± 54.89 [a]	214.41 ± 66.18 [b]	332.89 ± 126.44 [c]	**< 0.001**
Nuts (g/day)	6.66 ± 1.42 [a]	10.70 ± 1.39 [b]	12.68 ± 1.13 [b]	**0.006**
Legumes (g/day)	20.48 ± 11.07 [a]	26.40 ± 11.66 [b]	32.50 ± 17.54 [c]	**< 0.001**
Oil (g/day)	29.59 ± 4.29 [a]	29.51 ± 5.57 [a]	29.03 ± 7.45 [a]	0.795
Refined grains (g/day)	256.33 ± 111.29 [a]	225.32 ± 93.69 [a]	228.71 ± 88.52 [a]	0.080
Dairy (g/day)	164.67 ± 101.62 [a]	253.12 ± 165.30 [b]	315.19 ± 174.56 [c]	**< 0.001**
Meat (g/day)	34.49 ± 11.89 [a]	35.26 ± 12.86 [a]	42.72 ± 14.28 [b]	**< 0.001**
Sweets & sugar beverages (g/day)	25.43 ± 4.64 [a]	22.63 ± 4.85 [b]	9.49 ± 2.46 [b]	**0.013**

Abbreviations: kcal, kilocalorie; g, gram; SFA, saturated fatty acid; PUFA, polyunsaturated fatty acid; MUFA, monounsaturated fatty acid; RAE, retinol activity equivalents; mg, milligram; µg, microgram

Values are presented as mean ± SD

A one-way ANOVA test followed by Tukey's test was used

Welch's One-way ANOVA test followed by Tukey's test was used

Means with the same superscript letters (aa, bb, or cc) are not significantly different ($p > 0.05$)

suppressing oxidative stress, reduce bone resorption at the cellular level. They achieve by promoting osteoblast differentiation and viability, decreasing osteoblast apoptosis, enhancing osteocyte viability and reducing osteocyte apoptosis, and inhibiting osteoclast differentiation and viability [1].

Consumption of foods rich in phytochemicals is associated with increased serum phytochemical levels [31, 32]. It has also been shown that the consumption of seeds, nuts, legumes, vegetables, whole grains, and fruits elevates serum phytochemical levels [31]. Therefore, a phytochemical-rich diet boosts total carotenoid levels by reducing oxidative stress [6, 31]. On the other hand, greater intake of vegetables and fruits, which are rich sources of phytochemicals, ameliorates inflammation and oxidative stress [31, 33].

In this context, a phytochemical-rich diet improves inflammation and oxidative stress by reducing the production of pro-inflammatory cytokines, enhancing thermogenesis, inhibiting adipocyte differentiation, and reducing adipogenesis [9]. Also, phytochemicals decrease the activity of inflammatory factors, reduce oxidants including free radicals, increase mitochondrial oxidation, and suppress gluconeogenesis and fatty acid synthesis [31, 34–36]. These findings suggest that phytochemicals, due to their anti-oxidant and anti-inflammatory effects,

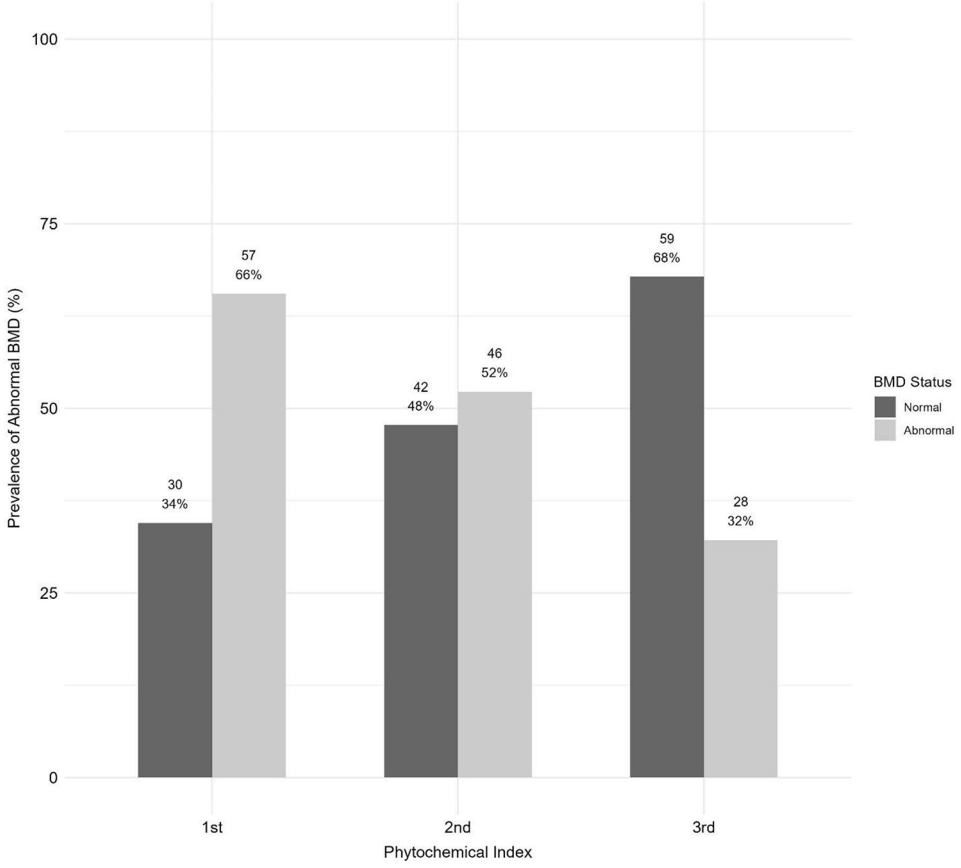

Fig. 1 The prevalence of abnormal BMD according to the tertiles of PI. Abbreviations: BMD, bone mass density; PI, phytochemical index. Using the chi-square test and values are frequency (percentage). *P-value was less than 0.001

along with receiving antioxidants such as vitamins A and C, play an important role in improving insulin resistance [37]. Results from various studies have reported that women with higher PI intakes experienced lower levels of oxidative stress, likely due to the interaction between sex hormones and the intake of certain phytochemicals, such as isoflavones with estrogen-like structures, which is consistent with our findings [37, 38]. Therefore, PI may have an inverse relationship with abnormal BMD.

In addition to these observations, the present study also demonstrated that greater consumption of fruits, vegetables, legumes, and nuts was related to a higher PI. Fruits and vegetables are known to be excellent sources of vitamins, minerals, dietary fiber, carotenoids, and flavonoids [39, 40]. Legumes are plant-based proteins rich in phytochemicals such as isoflavones, saponins, and phytosterols [39]. Nuts, too, possess antioxidant and anti-inflammatory properties due to their phytochemicals, including polyphenols, agititanine, and proanthocyanidins, as well as vitamin E and omega-3 [39, 41, 42], which contribute to their protective role against oxidative stress [39].

It is noted that dietary components account for 75% of OBS [16], meaning that modifying dietary habits—specifically, decreasing the intake of red and processed meats while increasing the intake of fruits, vegetables, legumes, and nuts— play a key role boosting OBS [16]. This aligns with the finding of the present study. Consistent with our findings, Shahriarpour et al. [16], indicated a significant relationship between higher OBS and increased bone mass in the lumbar spine. This was attributed to the lumbar spine's greater sensitivity to environmental factors, such as dietary intake and oxidative balance-related exposures [16, 43]. Thus, OBS may have anti-osteopenic and anti-osteoporotic effects in women by mitigating bone loss caused by oxidative stress. In this regard, adopting a diet rich in antioxidants and phytochemicals could be an effective strategy to improve bone health, particularly among at-risk populations such as postmenopausal women.

Focusing on phytochemical-rich foods, including olive oil, olive, seeds, nuts, legumes, whole grains, natural vegetable juices, vegetables, natural fruit juices, and fruits can improve DPI scores and reduce the risk of osteoporosis [44]. For example, adherence to the Mediterranean diet, which is rich in whole grains, legumes, fruits, and vegetables has been shown to support bone health [45]. Therefore, following the Mediterranean diet can lead to

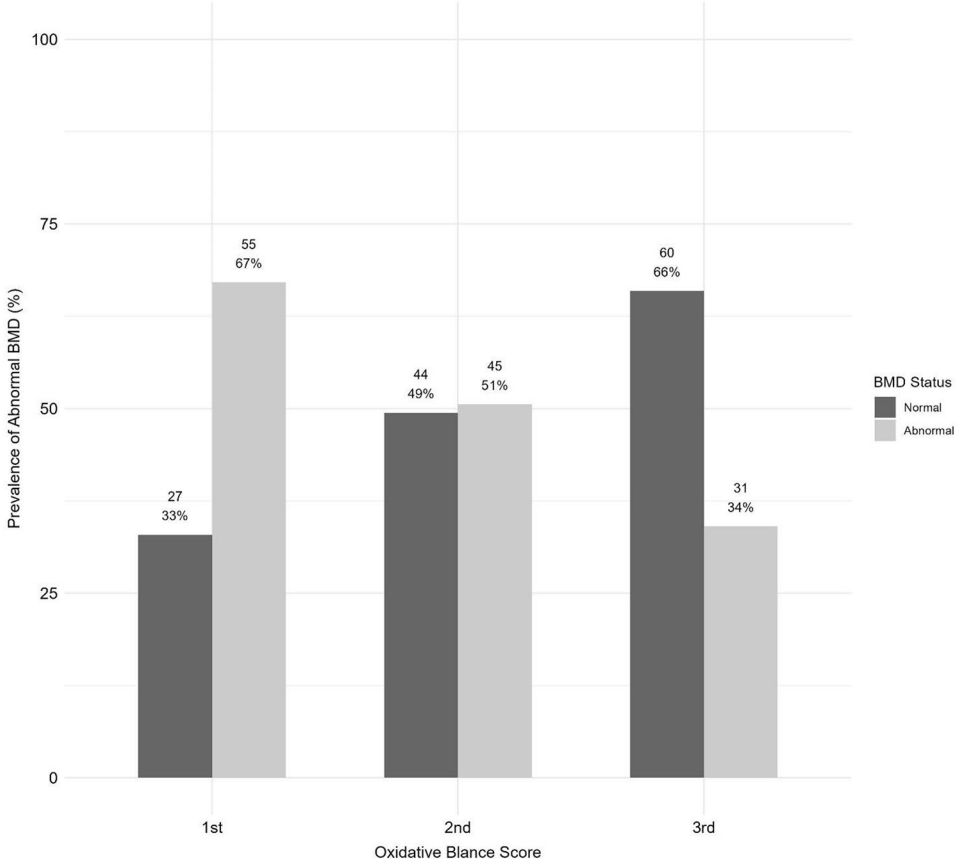

Fig. 2 The prevalence of abnormal BMD according to the tertiles of OBS. Abbreviations: BMD, bone mass density; OBS, oxidative balance score. Using the chi-square test and values are frequency (percentage). *P-value was less than 0.001

Table 5 Correlation between femoral and lumbar bone mineral density with phytochemical and oxidative balance score

Variables		Femoral BMD	Lumbar BMD
PI	Pearson Correlation	0.144	0.282
	P-value	**0.020**	<0.001
OBS	Pearson Correlation	0.247	0.291
	P-value	**<0.001**	**<0.001**

PI, phytochemical index; OBS, oxidative balance score; BMD, bone mass density

* Obtained from Pearson correlation

Significant values are shown in bold

higher PI and OBS scores, suggesting to help prevent osteoporosis.

This highlights the protective impact of vegetable and fruit intake on optimal bone health. However, the impact of certain dietary components found in fruit and vegetables, such as oxalates and phytates, may negatively affect calcium absorption, leading to more complex effect on bone health. For example, oxalate, which is present in vegetables such as spinach, interacts with calcium to create calcium oxalate, a compound characterized by its low solubility [46]. Similarly, phytate, present in soybeans, binds to calcium in the stomach, forming a water-soluble complex of calcium-phytate that decreases calcium absorption [46, 47]. Therefore, future research should focus on evaluating these interactions [7].

This is the first research to assess the link between the PI and OBS with the odds of abnormal BMD. However, our study has several limitations. First, while a valid FFQ was used to accurately estimate main exposure, recall bias remains a concern in case-control studies. Second, the limited sample size in this study may have impacted the significance of our findings. Also, some potential confounding variables, such as having a family history of osteoporosis, thyroid diseases, smoking (including hookah use), and use of other medications for various conditions, were not examined. Future research could benefit from investigating the link between dietary intake and the risk of bone disorders using longitudinal study designs.

Conclusions

Overall, the present study highlights the potential and important role of the PI and OBS potential in relation to abnormal BMD. The results indicate that higher PI and OBS are inversely associated with the odds of abnormal BMD. However, additional studies are necessary to investigate the underlying mechanisms, particularly how

Table 6 Association between phytochemical index and oxidative balance score with abnormal bone mineral density

Variables	Crude Model	Adjusted Model 1	Adjusted Model 2
	OR (CI 95%)	**OR (CI 95%)**	**OR (CI 95%)**
PI total score (energy %)	**0.96 (0.94, 0.98)**	1.043 (0.97, 1.11)	**0.96 (0.94, 0.98)**
P–value	<**0.001**	0.246	**0.001**
PI tertiles (energy %)			
T_1 (≤ 20.56 energy %)	Ref.	Ref.	Ref.
T_2 (20.57–31.34 energy %)	0.57 (0.31, 1.05)	0.56 (0.30, 1.04)	0.61 (0.32, 1.18)
T_3 (≥ 31.35 energy %)	**0.25 (0.13, 0.46)**	**0.23 (0.12, 0.44)**	**0.28 (0.14, 0.55)**
P_{trend}	<**0.001**	<**0.001**	<**0.001**
OBS total score	**0.87 (0.83, 0.92)**	**0.87 (0.82, 0.92)**	**0.88 (0.83, 0.93)**
P–value	<**0.001**	<**0.001**	<**0.001**
OBS tertiles			
T_1 (≤ 14)	Ref.	Ref.	Ref.
T_2 (15–19)	**0.50 (0.27, 0.93)**	**0.49 (0.26, 0.93)**	0.52 (0.26, 1.03)
T_3 (≥ 20)	**0.25 (0.13, 0.47)**	**0.24 (0.13, 0.46)**	**0.26 (0.13, 0.52)**
P_{trend}	<**0.001**	<**0.001**	<**0.001**

OR, odds ratio; CI, confidence interval; PI, phytochemical index; T, tertile

Model 1: adjusted for BMI and age

Model 2: additionally, adjusted for income, education, physical activity, calcium, and vitamin D supplement

These values are odds ratios (95% CIs)

* Obtained from logistic regression

Significant values are shown in bold

specific phytochemicals modulate signaling pathways related to osteoclastogenesis and osteoblast differentiation, especially in the context of oxidative stress-induced bone loss. Additionally, clinical trials evaluating specific dietary interventions rich in phytochemicals are recommended to determine their efficacy in improving bone health.

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Author contributions
M.M, F.S, A.S.H, M.G, and M.N; Contributed to data collection and writing the first draft. M.N and Z.S; Contributed to all data and statistical analysis and interpretation of data. M.N, B.P.G, and Z.S; Contributed to the research concept, supervised the work, and revised the manuscript. B.P.G contributed to funding acquisition and project administration. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The present study was approved by the Research Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran (IR.TBZMED.REC.1400.114). Informed consent was obtained from all participants. All methods conducted in this study were in accordance with the principles outlined in the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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