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# Major dietary patterns and kidney stone formation among Iranian men

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## ABSTRACT

**Objective:** To evaluate the association between major dietary patterns and the risk factors for kidney stone formation among Iranian men.
**Methods:** This cross-sectional study was conducted on 264 adult men, aged 19-89 years. The usual dietary intake of the participants over the previous year was collected using a validated semiquantitative food frequency questionnaire. Anthropometric measurements were recorded and 24-h urine samples were collected. Binary logistic regressions were used to evaluate the associations.
**Results:** The three major dietary patterns identified were healthy, unhealthy and spice-caffeine dietary patterns. After adjustment for age, BMI, and energy intake, the odds ratio (OR) of hypocitraturia in the second (OR = 0.57, 95% CI = 0.24-1.39, $p = 0.22$) and the third (OR = 0.24, 95% CI = 0.10-0.56, $p = 0.001$) tertiles, and the odds of hypercalciuria in the second (OR = 0.38, 95% CI = 0.17-0.87, $p = 0.022$) and the third (OR = 0.20, 95% CI = 0.10-0.46, $p < 0.001$) tertiles of the healthy dietary pattern decreased compared to the first tertile. The hypocitraturia in the second (OR = 1.14, 95% CI = 0.56-2.32, $p = 0.71$) and the third (OR = 5.14 95% CI = 2.04-12.96, $p = 0.001$) tertiles, the hypercalciuria in the second (OR = 0.67, 95% CI = 0.35-1.36, $p = 0.28$) and the third tertiles (OR = 4.11, 95% CI = 1.77-9.56, $p = 0.001$) of the unhealthy dietary pattern increased compared to the first tertile. The urine levels of creatinine, oxalate, and urea showed no significant association with healthy or unhealthy dietary patterns.
**Conclusion:** High adherence to the unhealthy and spice-caffeine dietary patterns and lower adherence to the healthy dietary pattern were associated with increased risk of kidney stone formation in men.

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## Introduction

Several studies have shown the globally increasing incidence of urinary stones during the previous decade [1]. The lifetime prevalence of symptomatic nephrolithiasis is approximately

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10% for men and 5% for women [2, 3]. The dietary intake is thought to be an important risk factor for kidney stone formation, although evidence is limited. Animal protein in our dietary intake could lead to increased urinary excretion of calcium and uric acid and decreased urinary citrate and urine pH, which together could result in the formation of calcium oxalate and uric acid stones [4]. Approximately, 80% of kidney stones contain calcium, and the majority of calcium stones consist primarily of calcium oxalate [5]. A large amount of urinary oxalate is derived from the endogenous metabolism of glycine, glycolate, hydroxyproline, and dietary vitamin C [6]. The contribution of dietary oxalate to urinary oxalate is unclear (estimates range from 10% to 50% [7]).

Dietary studies often focus on food items; however, it is better to consider dietary intake as a whole. For example, calcium intake may modulate the intestinal absorption of dietary oxalate [8]. According to observational studies indicating an inverse relationship between dietary calcium and the risk of kidney stones formation [9, 10], it is suggested that the dietary calcium could bind to oxalate in the gut, resulting in limited intestinal oxalate absorption and subsequent urinary oxalate excretion [11-13].

The dietary pattern approach has received great attention in recent years, specifically in relation to chronic diseases [14, 15], systemic inflammation [16], cardiovascular diseases [17], diabetes [18, 19], metabolic syndromes [20, 21], blood pressure [22], and obesity [23]. Despite several studies in Western countries, to our knowledge, there has been no study to assess the association between dietary patterns and urinary stone formation in an Asian population [8, 9, 24]. In this study, our main objective was to examine the relationship between major dietary patterns and kidney stone formation in a group of Iranian adult men.

## Subjects and methods

### *Subjects*

This cross-sectional study was conducted on 264 apparently healthy male individuals, aged 18-89 years, in the city of Tehran from September to December 2016. Our subjects were recruited from Urology Research Center of Sina Hospital, affiliated to Tehran University of Medical Sciences. Convenience sampling method was utilized to select the subjects. They received a brief explanation of the research through telephone and signed the informed consent form in the clinic.

**Table 1. Distribution of base characteristics**

| Variables | Group | n | % |
|---|---|---|---|
| **Marital Status** | Married | 241 | 91.3 |
| | Single | 23 | 8.7 |
| **Education** | Primary | 44 | 16.7 |
| | $6^{th}$ to $10^{th}$ Grade | 63 | 23.9 |
| | Diploma | 94 | 35.6 |
| | University | 63 | 23.9 |
| **Occupation** | Employee | 73 | 27.7 |
| | Retired | 47 | 17.8 |
| | Self-employed | 77 | 29.2 |
| | Worker | 60 | 22.7 |
| | Unemployed | 7 | 2.6 |
| | **Mean** | **SD** | **Range** |
| **Age (year)** | 42.68 | 12.67 | 19-89 |
| **BMI (kg/m$^2$)** | 26.75 | 3.98 | 17.30-41.35 |

The participants with a history of cardiovascular disease, diabetes, cancer, and stroke were excluded because of the possible variation in their diets. We also excluded individuals who left > 70 items blank in the food frequency questionnaire (FFQ), reported a total daily energy intake outside the range of 800-4200 kcal, or were on medications such as diuretics, corticosteroids, vitamin C and D supplements, calcium, or potassium citrate. The protocol of this study was approved by the Ethics Committee of Tehran University of Medical Science (TUMS).

### *Assessment of dietary intake*

Usual dietary intake was assessed using a validated 168-item semi-quantitative FFQ. A trained dietitian administered all the questionnaires. The FFQ consisted of a list of food items with standard serving sizes based on the Iranians' food consumption habits. Participants were asked to report the consumption frequency of a given serving for each food item during the previous year on a daily (e.g., bread), weekly (e.g., rice and meat), or monthly (e.g., fish) basis. The reported frequency for each food item was then converted to daily intake. Portion sizes of consumed foods were converted to common household measures [25].

### *Biochemical measurements*

A 24-h urine collection was done and samples

Table 2. Descriptive statistics of kidney stone formation risk factors

| Variables | Normal Range | Normal N (%) | Mean | SD | Median | IQR | Range |
|---|---|---|---|---|---|---|---|
| Creatinine (mg/dL) | 18-24 | 42 (15.9) | 26.5 | 8.0 | 26.4 | 3.71 | 7.9-88.7 |
| Citrate (mg/dL) | > 450 | 52 (19.7) | 350.9 | 157.5 | 321 | 177.7 | 53.7-1036 |
| Oxalate (mg/dL) | 20-40 | 101 (38.3) | 46.0 | 19.2 | 44.1 | 26.9 | 10-102 |
| Uric Acid (g/dL) | < 0.8 | 83 (31.4) | 857.6 | 277.8 | 899 | 259.6 | 84-1548 |
| Calcium (mg/dL) | < 250 | 67 (25.4) | 329.0 | 130.4 | 320.3 | 162.9 | 48-813.5 |

were analyzed for calcium, citrate, oxalate, creatinine, and uric acid using the AutoAnalyzer. Uric acid was measured with TOOS enzymatic colorimetric method. Urine creatinine concentration was measured using the Jaffe method, an enzymatic colorimetric method without removal of proteins. In this method, two reagents are used to identify the creatinine level and the wavelength corresponds to the concentration of creatinine. To measure the calcium level, the quantitative detection kits for cresolphthalein complex and photometric method were used. In this assay, calcium forms a violet-colored complex with cresolphthalein complexone in an alkaline medium. The color intensity indicates the calcium level. Citrate and oxalate concentrations were determined with spectrophotometry. In this method, each molecule absorbs the light at a specific wavelength.

*Assessment of other variables*

The socio-demographic data, including age, marital status, education, and occupation, were collected via an interview. Weight was measured to the nearest 100 grams using a digital scale, with participants wearing light clothing and no shoes. Height was measured using a measuring tape in a standing position, without shoes, while the shoulders were in a normal position. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.

*Statistical analysis*

The frequency (%) for categorical variables and mean ± SD, median, and 1st and 3rd quartiles for continuous variables were reported as descriptive statistics. Exploratory factor analysis (EFA) was conducted to extract major dietary patterns based on the 26 food groups. Principal components analysis and orthogonal varimax rotation were used to detect the number of dietary patterns and compute factor loadings, respectively. After computing factor scores, the relationship between dietary patterns and biochemical risk factors was evaluated with chi-square tests. The odds ratios (ORs) and 95% confidence intervals (CIs) of abnormal status for biochemical factors affected by dietary patterns were calculated using binary logistic regression models. The OR (95% CI) was calculated for each biochemical factor affected by dietary patterns. Statistical analyses were done using SPSS, version 24 (Chicago, IL) and a p value < 0.05 was considered as significant.

*Ethical approval*

The study was approved by the institutional ethics committee of Tehran University of Medical Science (ID: IR.TUMS.VCR.REC.1395.1046).

## Results

*Descriptive statistics*

The participants' clinical characteristics and laboratory data are summarized in Table 1 and Table 2, respectively. The final study sample comprised 264 men with a mean age of 42.68 ± 12.67 years, and BMI of 26.85 ± 3.98 kg/m2. Among them, 241 cases (91.3%) were married, 63 cases (23.8%) were university graduates and 29.2% were self-employed. The mean creatinine level was 26.5 mg/L, and only 42 cases (15.9%) had normal urine creatinine levels (Table 2). The mean citrate, oxalate, and calcium levels were 9.35, 0.45, and 0.33 mg/L, respectively. Normal urine levels of citrate, oxalate, and calcium were observed in 19.7%, 38.3%, and 25.4% of subjects, respectively. The mean uric acid concentration was 6.86 mg/L, and 31.4% had normal urine calcium level.

*EFA and dietary patterns*

Table 3 shows the EFA results for dietary patterns analysis. The factor loadings were reported as a measure of association between dietary patterns and food groups and the loadings below 0.3 were removed from the table.

Based on an eigenvalue greater than 2, three major dietary patterns including an unhealthy

**Table 3. Factor loadings matrix for the three dietary patterns identified using factor analysis**

| | Dietary Patterns | | |
|---|---|---|---|
| **Food Groups** | **Unhealthy** | **Healthy** | **Spice-Caffeine** |
| Sweet and dessert | 0.793 | | |
| Coke and drinks | 0.762 | | |
| Fast food | 0.722 | | |
| High-fat dairy | 0.696 | -0.345 | -0.315 |
| Junk food | 0.625 | | |
| Refined grains | -0.615 | -0.414 | |
| Nuts | 0.575 | | |
| Innards | 0.501 | | |
| Red meat | 0.474 | -0.304 | |
| High-oxalate vegetables | -0.536 | | |
| Egg | | | |
| Pickles | | | |
| Medium-oxalate vegetables | | 0.781 | |
| Legumes | | 0.747 | |
| Solid oil | | -0.634 | -0.460 |
| Fruit | | 0.634 | |
| Juice | | 0.624 | |
| Salt | | -0.605 | |
| Low-oxalate vegetables | | 0.574 | |
| Whole grains | | 0.532 | |
| Low-fat dairy | -0.431 | 0.528 | 0.352 |
| Chicken | | 0.496 | |
| Liquid oil | | 0.314 | |
| Cacao | | | 0.925 |
| Spice | | | 0.925 |
| Caffeine | | | 0.707 |
| **Eigenvalues** | 4.85 | 4.24 | 2.84 |
| **Explained variance** | 18.66 | 16.30 | 10.91 |

dietary pattern (UDP), a healthy dietary pattern (HDP), and a spice-caffeine dietary pattern (SCDP) were determined. The total explained variance was 48.87% and the KMO of 0.79 showed the sample size adequacy for EFA.

Based on factor loadings, the food groups of sweets-desserts, coke-fizzy drinks, and fast foods were the essential determinants of UDP. Average oxalate-containing vegetables, grains, and solid oils had the greatest loading to HDP, and SCDP was heavily loaded with cacao, spices, and caffeine.

*Relationship between dietary patterns and biochemical factors*

The frequency (%) of the abnormal status of kidney stone risk factors across dietary pattern score tertiles and the chi-square test results for evaluating the primary association between the risk factors and dietary patterns are displayed in Table 4. There was a significant decrease in hypercalciuria prevalence (from 88.5% to 62.5%, $p < 0.001$) and hypocitraturia prevalence (from 89.7% to 69.3%, $p = 0.003$) with increasing HDP tertile.

The prevalence rates of hypocitraturia and hypercalciuria in the third tertile of UDP were significantly higher than those in the first tertile (92.0% vs 71.6%, $p = 0.002$; 88.6% vs 69.3%, $p = 0.001$, respectively). Besides, we found significantly lower prevalence rates for hyperoxaluria and hypercalciuria in the 3rd vs 1st tertile of SCDP (51.1% vs 72.7%, $p = 0.01$, and 64.8% vs 81.8%, $p = 0.03$, respectively). None of the extracted dietary patterns showed a significant association with urine levels of creatinine ($p = 0.22$ for HDP, $p = 0.17$ for UDP, and $p = 0.09$ for SCDP) or uric acid ($p = 0.19$ for HDP, $p = 0.18$ for UDP, and $p = 0.26$ for SCDP).

The results of binary logistic regression to assess the effect of dietary pattern on the biochemical risk factors for kidney stone formation are displayed in Table 5. The first tertile of each dietary pattern was considered as the reference and the ORs (95% CI) were calculated for the abnormal status of risk factors. The effects of age, BMI, physical activity, and

**Table 4. Frequency of abnormal status of kidney stone risk factors across dietary pattern score tertiles**

| Dietary Pattern | Tertile | Abnormal Creatinine N (%) | Hypocitraturia N (%) | Hyperoxaluria N (%) | Hyperuricosuria N (%) | Hypercalciuria N (%) |
|---|---|---|---|---|---|---|
| **Healthy** | 1 | 78 (89.7) | 78 (89.7) | 47 (54.0) | 96 (75.9) | 77 (88.5) |
| | 2 | 72 (80.9) | 73 (82.0) | 60 (67.4) | 57 (64.0) | 65 (73.0) |
| | 3 | 72 (81.8) | 61 (69.3) | 56 (63.6) | 58 (65.9) | 55 (62.5) |
| | **P#** | 0.22 | 0.003 | 0.17 | 0.19 | < 0.001 |
| **Unhealthy** | 1 | 69 (78.4) | 63 (71.6) | 54 (61.4) | 54 (61.4) | 61 (69.3) |
| | 2 | 75 (85.2) | 68 (77.3) | 50 (56.8) | 62 (70.5) | 58 (65.9) |
| | 3 | 78 (88.6) | 81 (92.0) | 59 (67.0) | 65 (73.9) | 78 (88.6) |
| | **P#** | 0.17 | 0.002 | 0.34 | 0.18 | 0.001 |
| **Spice-caffeine** | 1 | 76 (86.4) | 76 (86.4) | 45 (51.1) | 61 (69.3) | 57 (64.8) |
| | 2 | 78 (88.6) | 69 (78.4) | 54 (61.4) | 65 (73.9) | 68 (77.3) |
| | 3 | 68 (77.3) | 67 (76.1) | 64 (72.7) | 55 (62.5) | 72 (81.8) |
| | **P#** | 0.09 | 0.20 | 0.01 | 0.26 | 0.03 |

# Chi square test

**Table 5. Logistic regression results: odds ratios (95% confidence interval) of the abnormal status of kidney stone formation risk factors affected by dietary patterns**

| Dietary Pattern | Tertile | Creatinine OR (95% CI) | P | Citrate OR (95% CI) | P | Oxalate OR (95% CI) | P | Uric Acid OR (95% CI) | P | Calcium OR (95% CI) | P |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Healthy** | | . | 0.16# | . | 0.001# | . | 0.15# | . | 0.08# | . | <0.001# |
| | 2 | 0.54 (0.22- 1.33) | 0.18 | 0.57 (0.24-1.39) | 0.22 | 1.77 (0.94-3.32) | 0.08 | 0.66 (0.32-1.35) | 0.25 | 0.38 (0.17-0.87) | 0.02 |
| | 3 | 0.51 (0.20-1.29) | 0.16 | 0.24 (0.10-0.56) | 0.001 | 1.55 (0.83 -2.92) | 0.17 | 0.51 (0.02-1.07) | 0.07 | 0.20 (0.10-0.46) | <0.001 |
| **Unhealthy** | | . | 0.04# | . | 0.001# | . | 0.31# | . | 0.03# | . | 0.002# |
| | 2 | 1.34 (0.58-3.07) | 0.50 | 1.14 (0.56-2.32) | 0.71 | 0.89 (0.48-1.67) | 0.72 | 1.02 (0.05-2.08) | 0.98 | 0.67 (0.35-1.36) | 0.28 |
| | 3 | 2.50 (1.03-6.07) | 0.06 | 5.14 (2.04-12.96) | 0.001 | 1.43 (0.76-2.72) | 0.27 | 2.24 (1.09-4.60) | 0.07 | 4.11 (1.77-9.56) | 0.001 |
| **Spice-Caffeine** | | . | 0.06# | . | 0.09# | . | 0.001# | . | 0.22# | . | 0.02# |
| | 2 | 0.97 (0.38-2.47) | 0.94 | 0.54 (0.24-1.22) | 0.14 | 1.69 (0.90-3.18) | 0.10 | 0.10 (0.47-2.01) | 0.93 | 1.61 (0.81-3.21) | 0.18 |
| | 3 | 0.46 (0.20-1.06) | 0.07 | 0.50 (0.23-1.11) | 0.10 | 2.90 (1.51-5.60) | 0.001 | 0.64 (0.31-1.29) | 0.21 | 2.4 1(1.17-4.95) | 0.02 |

# P value for trend
The model is adjusted for age, BMI, physical activity, and energy intake.

energy intake were adjusted.

HDP significantly decreased the urine levels of citrate ($p = 0.001$) and calcium ($p < 0.001$) since the ORs of hypocitraturia in the second and third tertiles of HDP were 0.57 (95% CI = 0.24-1.39, p = 0.22) and 0.24 (95% CI = 0.10-0.56, p = 0.001), respectively, and the ORs of hypercalciuria in the second and third tertiles of HDP were 0.38 (95% CI = 0.17-0.87, p = 0.02) and 0.20 (95% CI = 0.10-0.46, p = 0.001), respectively.

We observed a significant incremental effect of UDP on urine citrate (p = 0.001) and calcium levels (p = 0.002) as the ORs of hypocitraturia in the second and third tertiles of the unhealthy pattern were 1.14 (95% CI = 0.56-2.32, p = 0.71) and 5.14 (95% CI = 2.04-12.96, p = 0.001), respectively. The ORs of hypercalciuria in the second and third tertiles of UDP were 0.67 (95% CI = 0.35-1.36, p = 0.28) and 4.11 (CI = 1.77-9.56, p = 0.001), respectively.

In addition, SCDP significantly increased the urine levels of oxalate (p = 0.001) and calcium (p = 0.02). The ORs of hyperoxaluria in the second and third tertiles of this dietary pattern were 1.69 (95% CI = 0.90-3.18, p = 0.10) and 2.90 (95% CI = 1.51-5.60, p = 0.001), respectively. Also, the ORs of hypercalciuria in the second and third tertiles of SCPD were 1.61 (95% CI = 0.81-3.21, p = 0.18) and 2.41 (95% CI = 1.17-4.95, p = 0.02), respectively.

There were no significant adjusted association between the healthy (p = 0.16) and spice-caffeine (p = 0.06) dietary patterns and urine creatinine level, although the odds of abnormal creatinine level showed a significant increasing trend from the first to third tertile (p = 0.04).

## Discussion

The aim of this study was to evaluate the association of major dietary patterns with kidney stone formation among healthy male individuals. Our results revealed a relationship between dietary patterns and 24-h urinary levels of citrate, oxalate, and calcium.

In the present study, the healthy dietary pattern (HDP) comprised legumes, vegetable, fruits, juice, whole grains, and low-fat dairy plus lower intake of salt, refined grains, and solid oils. The unhealthy dietary pattern (UDP) was characterized by desserts, sweets, coke and fizzy drinks, fast food, high-fat dairy, and junk food.

We found that urinary citrate level was significantly influenced byboth HDP and UDP. HDP was associated with higher citrate excretion, while UDP was related to lower citrate excretion. The odds of hypocitraturia was decreased by following HDP or avoiding UDP. According to Han et al., lower urinary citrate could cause renal tubular acidosis, which leads to the formation of kidney stones [26].

In the current study, following HDP resulted in increased urinary citrate level, and this is inconsistent with Ferraro et al., who showed that consumption of sufficient liquid and high amounts of fruits and vegetables was related to an overall decrease in kidney stone formation [24].

According to our data, the urinary calcium level was associated with all major dietary patterns (HDP, UDP, and SCP). By following HDP, the odds of hypercalciuria levels, and subsequently the risk of kidney stone formation, decreased. Moreover, according to previous reports, the consumption of salt, sugar, sweetened drinks, and refined grains could increase the urinary calcium excretion [27, 28], and the higher consumption of sodas and sweetened drinks could lead to kidney stone formation [24, 29]. We observed that the odds of hypercalciuria was increased due to the high level of SCDP. Consistently, it was shown that coffee and tea, as the caffeine source, could lead to increased urinary calcium excretion [30, 31].

Consistent with our results, regarding the increased odds of hyperoxaluria and hypercalciuria, Massey et al. reported higher hyperoxaluria by increasing the tea and chocolate consumption [32]. Also, turmeric supplementation significantly increased the risk of kidney stones formation [33].

It was shown that consuming caffeine alone could reduce the risk of kidney stone formation. We also found that consuming more tea and coffee could increase the urinary volume in our subjects. Nevertheless, the anti-inflammatory and anti-oxidant properties of tea might have resulted in lower kidney stone formation. It has also been mentioned that the results could be different if the participants had a history of kidney stones [30].

Based on our data, urinary creatinine level showed no significant relationship with HDP, UDP, or SCP, although the prevalence of abnormal creatinine level decreased with increasing adherence to HDP and tended to increase with increasing adherence to UDP. In one cohort study, there was a nonsignificant relationship between the consumption of nondairy animal protein and the risk of kidney stone formation [34]. Moreover, One study showed that higher protein consumption could increase the acidic load of urine and the urinary excretion of uric acid, leading to kidney stone formation [35].

The cross-sectional design of this study was one of its limitations since it did not reveal any causal relationship. Thus, longitudinal studies are suggested as a further attempt. Another limitation was the small sample size of the study. In addition, since all of our participants were male, more studies are needed in both genders to compare the results between them. This study was the first attempt to investigate the relationship between dietary patterns and urinary biochemical parameters as the risk factors for kidney stone formation. High adherence to either an unhealthy or a spice-caffeine dietary pattern and lower adherence to a healthy dietary pattern could increase the risk of kidney stone formation in men. Further studies are warranted to clarify the association between dietary patterns and the possibility of kidney stone formation.

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## Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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