

Evaluation of the Dietary Risk Factors in Calcium Oxalate Stone Forming Cases in Turkey

Türkiye'deki Kalsiyum Oksalat Taşı Vakalarının Diyet Risk Faktörleri Açısından Değerlendirilmesi

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ABSTRACT

Aim: To evaluate the dietary content and evaluate the possible related risk factors in patients with calcium oxalate (CaOx) stones

Material and Method: A total of 2348 patients with CaOx stone disease and 1024 cases with no signs of stone disease were evaluated concerning the possible dietary content-related risk factors for stone formation. A well-prepared comprehensive questionnaire focused on the diet-related risk factors including fluid intake, sodium, animal protein, black tea, fruit juice, coffee, and vegetables was utilized. Urinary risk factors have been identified and additionally, the patient-related factors and possible effects of physical exercise, and smoking were also well evaluated.

Results: Evaluation of our findings demonstrated that 46.2% of study group cases consumed water less than 1 liter per day; black tea consumption was also found to be higher (28.9% consuming black tea >451 cc/day) in cases with CaOx stones. Similarly, consumption of daily coffee, protein, salt, and dairy products was higher in these cases than in the control group. Also, daily physical activity amounts were lower in this group of patients. Lastly, urinary stone-forming risk factors were common in patients with CaOx stone disease.

Conclusion: When comparing calcium-containing stones to others, our findings revealed that high salt, black tea, and animal protein consumption were the main stone-forming risk factors. These patients had higher levels of urinary risk factors than the general population.

Key words: calcium; oxalate; kidney; stone; diet

ÖZET

Amaç: Kalsiyum oksalat (CaOx) taşı olan hastalarda diyet içeriğini değerlendirmek ve ilişkili olası risk faktörlerini değerlendirmek

Materyal ve Metot: CaOx taş hastalığı olan toplam 2348 hasta ve taş hastalığı belirtisi olmayan 1024 vaka, taş oluşumu için diyet içeriğine bağlı olası risk faktörleri açısından değerlendirildi. Sıvı alımı, sodyum, hayvansal protein, siyah çay, meyve suyu, kahve ve sebzeleri içeren diyetle ilişkili risk faktörlerine odaklanan iyi hazırlanmış kapsamlı bir anket kullanıldı. Üriner risk faktörleri tanımlanmış ve ayrıca hastaya bağlı faktörler, fiziksel egzersiz ve sigara içmenin olası etkileri de iyi değerlendirilmiştir.

Bulgular: Bulgularımız değerlendirildiğinde, çalışma grubu vakalarının %46,2'sinin günde bir litreden az su tükettiği; CaOx taşı bulunan olgularda siyah çay tüketiminin de daha yüksek olduğu (%28,9 siyah çay tüketimi >451 cc/gün) saptanmıştır. Benzer şekilde bu olgularda günlük kahve, protein, tuz ve süt ürünleri tüketiminin kontrol grubu olgularına göre daha yüksek olduğu görüldü. Ayrıca bu hasta grubunda günlük fiziksel aktivite miktarları daha düşüktü. Son olarak CaOx taş hastalığı olan hastalarda üriner sistem taşı oluşturan risk faktörleri yaygındı.

Sonuç: Kalsiyum içeren taşları diğer taşlarla karşılaştırdığımızda bulgularımız yüksek tuz, siyah çay ve hayvansal protein tüketiminin taş oluşumuna neden olan ana risk faktörleri olduğunu ortaya koydu. Bu hastalarda genel popülasyona göre daha yüksek düzeyde üriner risk faktörleri vardı.

Anahtar kelimeler: kalsiyum; oksalat; böbrek; taş; diyet

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Urolithiasis prevalence has increased in several regions of the world, with significant changes in disease-related characteristics during the last three decades. In addition to significant changes in food habits and attitudes, developments in the identification and minimally invasive therapy of urinary stones in instances with urinary stones have also contributed to these changes¹⁻⁴.

Parallel to the increase in prevalence, reported data demonstrated that time-dependent stone recurrence rates also increased (31.5–50% for five and 72% in twenty years respectively)^{5,6}. These observations regarding the increased risk of new stone formation have led urologists to focus not only on the minimally invasive management approaches to render the patients stone-free but also the efficient preventive measures (metaphylaxis) to limit new stone formation risk, particularly in recurrent stone formers. Regarding the possible underlying risk factors responsible for urinary stone formation and subsequent recurrences, changes in dietary habits, particularly in the younger generation, have been regarded to be highly important in this aspect⁷⁻⁹. Although limited, outcomes of some well-designed studies with an adequate number of cases have demonstrated that in addition to fluid intake, consumption of some other dietary constituents including calcium, oxalate, carbohydrate, sodium, protein, etc. were also found to affect the urinary composition by increasing the excretion of urinary risk factors and that of subsequent supersaturation⁹⁻¹³ Related to the possible effects of dietary factors on stone formation although general evaluation and reported data seem to be useful, data derived from the local/regional epidemiological studies focusing on personal dietary and metabolic risk factors could be highly important to reflect the exact role of dietary habits in different parts of the world.

In this study, we wanted to examine the dietary risk factors that may be connected with the development of CaOx stones disease in a specific percentage of the Turkish population due to a lack of data on the prospective influence of various nutritional components on the risk of stone formation.

Method

To evaluate the possible relationship between dietary factors and the risk of calcium oxalate stone formation, a prospective observational study was conducted in 2348 adult patients (>18 years) with CaOx nephrolithiasis (Study group). From September 2019 to 145

June 2022, a questionnaire survey was conducted on adult patients referring to pre-diagnosed CaOx stone disease. Data obtained in these cases were compared with the findings of 1024 cases referring to complaints of other diseases without any history and evidence (diagnosis) of stone disease (Control group). Patients presenting with certain pre-diagnosed kidney disease (s), active UTI, and other metabolic problems were excluded from the study program. Additionally, cases with a history of diet-related restriction, gout, hyperparathyroidism, nephrocalcinosis, gastrointestinal disease, renal tubular acidosis, urologic anatomical abnormalities, or chronic renal failure were also excluded.

Before the inclusion of patients into the study program no evidence of stone disease was confirmed in control group cases (n: 1024) with a detailed anamnesis and appropriate radiological evaluation. Stone-forming risk factors by performing a 24-hour urine analysis were performed in all cases in both groups. An informed consent has been obtained from all cases after describing the aim of the trial and the type, and content of evaluations to be made (urine, blood, and radiological).

In close collaboration with epidemiologists, our team developed a simple yet thorough questionnaire. Each form was completed by nurses and resident doctors on the urology units, who conducted face-to-face interviews with research participants in the urolithiasis and control groups. Gender, age, BMI values, dietary habits, smoking status, prior stone events, interventions, related co-morbidities, and exercise conditions were among the questions on documented risk factors for urinary calculi.

In addition to the basic demographic characteristics, daily exercise conditions, and family history, regarding the dietary habits of the cases, apart from daily fluid intake, frequency and type of consumption of salt, animal protein, carbohydrate, dairy products, coffee, black tea, soda water, fruit juice, vegetables were carefully asked and recorded. Last but not least, urinary stone-forming risk factors were identified in 24-hour urine samples obtained from both group cases.

Statistical Analysis

Utilizing IBM Statistical Package for Social Sciences (SPSS) program version 17.0 (IBM, Chicago, IL, USA), the obtained data in both case groups were examined. The values were assessed for significance using a chi-square test, and the independent risk factors for urolithiasis were examined using multivariate logistic analysis. For statistical significance, a p-value of less than 0.05 was used.

Results

Evaluation of the data regarding dietary consumption as well as urinary stone-forming risk factors obtained in 2348 cases with CaOx stone disease and 1024 cases without any evidence of urolithiasis revealed the following findings;

While the male/female ratio was 1.35 in the study group (1346 males, 1002 females) this value was 1.20 in control group cases (559 males, 465 females). Median age of the population was 42.7 (range: 15–69) years and 40.8 (range: 21–66) years in both groups respectively. Stone analysis data was identified as CaOx in all cases. Body mass index (BMI) values were above 30 in 31.3% of the cases in Group 1 and 29.1% of Cases in Group 2.

As the most important preventive parameter, evaluation of daily fluid consumption in our cases demonstrated that while nearly half of the population evaluated (1086 cases, 46.2%) consumed water less than 1 liter per day in Group 1. 42.8% of the cases consumed 1–2 liters per day and unfortunately only 10.8% of the patients consumed more than 2 liters per day. On the other hand, however, 39.0% of the cases in Group 2 were found to consume more than 2 liters of water per day.

Among the other constituents of diet dairy proteins (milk, yogurt, etc.) consumption rate (>3 days/week) was significantly higher in study group cases (46.2% vs 37.5%) than in control group. Similarly, the dietary content of sodium (salt) was prominently higher in cases suffering from stone disease compared to those in the control group (Consumption regularly at every meal 46.6% vs 30.9%).

Of the other diet-related parameters evaluation of black tea consumption demonstrated the common consumption where 28.9%, of the cases in Group 1 consumed more than 451 cc/day. This value was 21.5% in control group cases (p: 0.024). While 35.5% of the cases consumed more than 2 coupes of coffee/day in Group 1 cases, this value was 25.7% in cases without stone disease. There was no statistically significant difference between both groups regarding cola consumption (10.8% vs 7.9% consumption of more than 2 glasses of cola/day), cigarette smoking, soda water, and vegetable consumption (Table 1).

Evaluation of physical activity status in both groups of cases demonstrated a significant difference where patients with stone disease seemed to have less activity (36.7% of the cases had exercise 1-3 days/ week) compared with the cases in Group 2 (19.8%). All constituents of diet and their daily consumption rates are given in Table 1.

Last but not least, evaluation of stone-forming risk factors in both groups of cases revealed higher excretion of relevant constituents (Calcium, Uric acid, oxalate) in patients with CaOx stones.

A summary analysis of our findings revealed a statistically significant (p<0.05) difference between the two groups of cases concerning the 13 variables identified including physical activity, BMI values, fluid intake, sodium intake, animal protein and dairy products consumption, black tea, and coffee consumption.

Table 1. Evaluation of dietary risk factors in both groups

	Study group		Control group		
	N	%	N	%	Р
Total number of cases	2348		1024		
Fluid consumption					
≤1 L/ day	1086	46.2	282	27.5	0.025
1–2 L/ day	1007	42.8	342	33.3	
≥2 L/ day	255	10.8	400	39.0	
Consumption of fruit					
Juice (1 glass=200 cc)					
None	1634	69.6	412	40.2	
≤200 cc/day	350	14.9	359	35.1	
≥200 cc/day	363	15.5	253	24.7	0.032
Consumption of black tea					
(1 tea glass: 50 cc, 1 large glass/c	oupe: 20)0 cc)			
None	218	9.3	108	10.6	0.25
≤150 cc/ day	700	29.8	327	31.9	0.024
151 – 450 cc /day ≥451 cc/day	750 680	32.0 28.9	368 221	35.8 21.5	
Consumption of coffee	000	20.0		21.0	
None	481	20.5	394	38.7	
≤1 coupe/ day	1033	44.0	366	35.6	
\geq 2 coupe/ day	833	35.5	264	25.7	0.045
Consumption of cola		0010	201	2011	01010
(1 glass=300 cc)					
None	1213	51.7	716	69.9	
≤1 glass /day	880	37.5	227	22.2	
≥2 glasses/day	255	10.8	81	7.9	0.045
Consumption of soda water					
(1 glass=200 cc)					
None	662	28.2	217	21.2	0.023
≤1 glass /week	857	36.5	462	45.2	
≥2 glasses/week	829	35.3	345	33.6	
Consumption of water (L/day)					
≤1 L/ day	1086	46.2	282	27.5	0.025
1–2 L/day	1007	42.8	342	33.3	
≥2 L/day	255	10.8	400	39.0	0.01
Consumption of animal protein/da	у				
6–7 days/week	842	35.9	226	22.1	0.025
4–5 days/ week	576	24.5	349	34.1	
<3 days/week	930	39.6	449	43.8	
p<0.05 significant.					_

Discussion

Changing lifestyles and dietary habits in the population have caused a prominent increase in the prevalence of stone disease over the past decades¹⁰. This issue, the lifetime risk of urolithiasis has been observed to range from 1-5% in Asia, 5-9% in Europe, 10-15% in the United States, and 20-25% in the Middle East, with Greenland and Japan having the lowest frequency⁵.

Although the underlying mechanisms involved in urinary stone formation are complex and multifactorial; data obtained in several studies have pointed out that the dietary habits and lifestyle of the major strategy for preventing the recurrence of urolithiasis-involved cases are important factors for close consideration^{11,12}. If left untreated at least 50% of these individuals will have recurrent stone formation. It is well known that the composition of urine is highly important for stone formation and this factor is partly dependent on diet, including mainly the amount of fluid intake. When it comes to dietary risk factors for calcium-containing stones, the majority of stones are made of calcium oxalate, accounting for 40-60%. In contrast, the data regarding non-calcium-containing stones is rather sparse¹³. Daily diet management was shown to be a preventive approach and has gained more and more importance in recent years^{14–16}.

As stated above composition of daily diet plays a major role in the concentration of several urinary solutes and inhibitors involved in the formation and growth of urinary calculi. Determining the impact of one's diet on future stone risk begins with a dietary history and subsequent metabolic evaluation to outline the presence and impact of such factors. Regarding the dietary factors affecting the urinary levels of stone-forming risk factors and subsequent stone formation as a result, previous studies have demonstrated well that high fluid is highly important to reduce the risk of stone formation^{17,18}. Increased urine volume has been demonstrated to lower the concentration of calcium oxalate in the urine and reduce the risk and recurrence rate of stone formation by 50% and 60–80%, respectively^{19,20}.

However, a number of randomized controlled studies evaluating the effects of fluid consumption on urinary risk factors as well as stone formation are highly limited and it is unknown whether all liquids (with different levels of hardness and constituents) have similar effects on the risk of stone formation. However, research has shown that some other liquids, such as orange juice, coffee, tea, wine, and beer, may lower the risk of stone development while carbonated and sugar-containing beverages may raise it^{17,21}.

In relation to this matter, it has been suggested that tea drinking may influence the excretion of risk factors for the development of stones, and prolonged tea drinking may raise the risk of stone formation by increasing oxalate intake. As a possible risk factor for hyperoxaluria, increased black tea consumption has been considered a risk factor particularly in recurrent stone-forming cases^{22–24}. On the other hand, contradictory information from a few recent research has shown that drinking tea, especially green tea, can help prevent the development of stones^{25–28}.

In addition to the fluid intake, however, some other certain dietary components have also been found to be responsible for the formation and recurrence of calcium-oxalate calculi. Of these dietary components, high sodium intake was found to be responsible for elevated urinary sodium excretion levels which will in turn inhibit calcium absorption in the renal tubules. Higher calcium excretion will induce hyperuricemia resulting in increased risk for calcium oxalate crystal formation²⁹. This topic is related to the findings of a study that examined the potential effects of sodium consumption levels on the formation of calcium oxalate stones in 210 patients. The study found that patients who present with hypercalciuric stones experience a significant decrease in calcium excretion when eating a low-salt diet (271 mg/day vs. 361 mg/day). This suggests that dietary salt intake may have an impact on the levels of calcium elimination and stone formation³⁰. In another trial, Sorensen et al. evaluated the relationship between dietary content related kidney stone formation and they were able to show that elevated dietary sodium intake will prominently increase the risk of nephrolithiasis by $11-61\%^{31}$. Similar studies have demonstrated the same correlation between higher salt consumption and urinary sodium and calcium excretion levels which has been reported to be linear^{15,29,32}.

Published data so far strongly emphasized that overconsumption of protein in daily diet, particularly animal protein, has been reported to be an important risk factor for new stone formation. Regarding this issue, in an animal model of increased protein intake, the authors were able to show that a high casein diet can cause a prominent increase in urinary calcium excretion where urinary citrate excretion and urinary pH were found to be relatively lower³³. Other clinical investigations by other authors also showed the protective benefits of limiting animal protein in a regular diet to lower the excretion of oxalate, phosphate, calcium, hydroxyproline, and uric acid. An increase in urine citrate excretion as a result of this dietary adjustment also reduced the incidence of stone formation^{34,35}.

As previously said, regulating fluid and nutritional consumption patterns is critical in the overall prevention of urolithiasis. Nonetheless, despite a huge amount of epidemiological data, high-quality prospective interventional research is scarce in this field. Taking this into consideration, the current observational study intended to investigate the underlying dietary risk factors in instances of urinary stones and compare the results to patients with no indications of stone illness.

Evaluation of the data obtained in our groups demonstrated the higher consumption of some well-established dietary stone-forming risk constituents in cases with urolithiasis. Patients with stone disease tended to consume more black tea, coffee, dairy products, salt, and animal protein than the cases without any evidence of stone disease. Physical activity was less in these cases with a more prominent sedentary life. Obesity was more common among the cases with urolithiasis and the rate of excreted urinary stone forming risk factors was significantly higher in these cases. Of these factors, higher excretion of oxalate and lower levels of citrate were the two common abnormalities noted in our group.

Based on all these factors, we may say such local, and regional epidemiological studies focusing on personal dietary and metabolic risk factors could be highly important in an attempt to derive valuable, predictive clinical implications to limit the risk of stone recurrence as well as lower the economic burden of the disease and outline the most rational treatment alternative.

Our study is not free of limitations. Number of patients evaluated may be limited. Again, some other certain dietary risk factors could be inquired and assessed. However, taking limited information regarding the epidemiological data on stone disease particularly in a regional evaluation-based manner, we believe our findings will be contributive enough on this aspect. Additionally, taking the endemic nature of the stone disease in our country, we believe that these values coming from a local regional part of a such country will give further insights into the epidemiologic features of the disease.

Conclusion

In the light of our current results and the published data so far confirm the importance of individual dietary factors in the development of calcium oxalate kidney stones. A well-evaluated dietary content is of paramount importance in an attempt to make the necessary modifications to lower the urinary excretion levels of stone-forming risk factors. Management of symptomatic urinary stones with minimally invasive stone removal procedures will not prove "complete" unless they are supported with metabolic evaluationbased dietary modification to reduce the urinary levels of stone-forming risk factors and subsequent stone formation.

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Authors' Contribution

The authors share the responsibility for the manuscript.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest

The authors declare no potential conflicts of interest regarding this article.

Disclaimer

The content is solely the responsibility of the authors.

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