Review Article

Impact of diet on renal stone formation

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Abstract

Background and Objectives: The incidence of kidney stones is increasing globally, with a preponderance in adults compared with that in adolescents and children. Dietary habits have been identified as significant contributing factors to kidney stone formation. This literature review aimed to explore the existing evidence on the impact of diet on renal stone formation. **Methods and Study Design:** We conducted a comprehensive literature review and included 81 studies published between 1999 and 2023, limiting the search to articles published in English. The extracted data were analyzed to identify common themes, trends, and patterns related to the impact of diet on renal stone formation. We investigated the influence of dietary habits on the risk of nephrolithiasis. **Results:** Although the role of fluid intake in relation to stone formation is clear, existing evidence on how different types of beverages (coffee, tea, fruit juices, and soft drinks) affect kidney stone formation is conflicting. Other factors such as protein, sodium chloride, calcium, oxalate, fat, and carbohydrate intake have also been discussed as contributors to nephrolithiasis. Thus, diet should be appropriately modified to reduce the risk of stone formation in susceptible individuals. A history of nephrolithiasis has been found to increase the risk of both chronic kidney disease and end-stage renal disease. The review acknowledges the limitations inherent in conducting a literature review, including the potential for publication bias and the reliance on available published studies. **Conclusions:** These findings highlight the importance of understanding and preventing nephrolithiasis.

Keywords: Dietary habits, fluid intake, kidney disease, kidney stones, nephrolithiasis

Introduction

The incidence of nephrolithiasis is increasing globally, and dietary habits have been identified as leading risk factors. Other factors include age, ethnicity, and sex (men).[1] The incidence of kidney stones is higher in adults than in children, and adolescents are at the highest risk of developing kidney stones.[2,3] A 25-year population study conducted in the United States involving patients older than 10 years of age found that most kidney stone cases occurred in adults, with only 4% occurring in adolescents.[4]

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The same study reported annual incidence rates of kidney stones of 36 per 100,000 women and 109 per 100,000 men. Although the reason for the difference in the incidence of nephrolithiasis between adults and children is not yet understood, some scholars suggest that it may be related to the increased availability of protective urinary citrate and magnesium in children.[5]

A higher risk of chronic kidney disease and end-stage renal disease has been reported in patients with a history of urolithiasis.[6,7] This highlights the importance of understanding renal stone formation and prevention measures. The kidney stones mainly comprise calcium oxalate (65%) and calcium phosphate (17%), with other components including uric acid, struvite, and cystine at 8%, 3%, and 0.4%, respectively.[8]

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Several factors contribute to kidney stone formation, including anatomical abnormalities, functional impairment, genetics, metabolism, and nutritional status.[9] Nutrition is a known modifiable risk factor in adults, with emphasis on fluid intake, pH, and diet composition.[10] Recent studies have provided conflicting evidence about the effects of certain nutritional components on nephrolithiasis. We believe this article is important for family physicians and general practitioners and address the importance of proper dietary habits in preventing renal stone formation Thus, this study aimed to explore the evidence in the literature regarding the impact of diet on renal stone formation.

Fluids

Reduced urinary volume leads to solvent saturation and promotes stone formation.[9,10] A pilot study conducted in 2016 analyzed urine osmolality and 24-hour urine of 100 steel plant workers in comparison to those of 15 healthy adults from another study conducted in the same region and 1061 men stone formers extracted from a medical registry.[11] The effect of outside temperatures was considered, with hot climate categorized as 40.5°C–54°C, while normal areas were those below 26.7°C. More than half of the workers were dehydrated, with a calculated urine osmolality of ≥700 mOsm, and 39% of the workers had spot urine osmolality >800 mOsm. The study found that increased urine osmolality was associated with increased urinary analytes for different types of renal stones as steel workers had higher urinary magnesium, calcium, sulfate, and phosphorus concentrations than the 15 healthy adults. Little difference was found in urine osmolality between workers in hot (687 mOsm) and normal environments (749 mOsm). One limitation in this study is that 24-hour urine collection included specimens collected outside working hours, thereby reducing reliability of samples as they intended to investigate the work environment (dehydration) on urine specimens. Another study with a similar design conducted in 2005 involving 10,326 steel workers identified 181 patients with kidney stone disease.[12] Of these 181 workers, an association between kidney stones and hot climate was identified as 103 worked in hot conditions and 78 worked at room temperature ($P < 0.001$). Low urinary volume was also more strongly associated with working in hot environments ($P = 0.01$). This retrospective cross-sectional paper had a larger population with more thorough exclusion criteria as only those with 3 or more years working history at the company were included. However, no females were included as they noted none worked at temperatures as high as those where men worked, which poses a limitation.

A meta-analysis of 50 articles published in 2020 investigated the primary prevention of nephrolithiasis. An intake of 2.0 L/day was reported to reduce the incidence of stones by nearly 50% compared to an intake of less than 1.0 L/day [risk ratio 0.56; 95% confidence interval (CI), 0.48–0.65].[13] Another meta-analysis of nine studies published in 2015 found that a urine volume of 2.0–2.5 L/day helps reduce the risk of renal stone recurrence.[14] Patients with cystinuria have a larger recommended fluid intake to ensure a urinary cysteine level of less than 250 mg/L (1.0 mmol/L) per day at a pH greater than 7.0.[15] The calculated optimal urinary output for this population was reported to be ≥3.0 L/day.[15,16] A summary of the recommended daily fluid intake according to age is presented in Table 1.[17,18]

Fruit juices

The citrate content in fruit juice affects the urinary pH and citrate excretion. Urinary citrate binds to calcium, thereby impairing formation of calcium crystals.[19,20] Moreover, the metabolism of alkali citrate to bicarbonate increases urinary pH and citrate excretion, suggesting that citrus fruit juices protect against renal stone formation.[21] A prospective study by Pietro Ferraro *et al.*[22] analyzed three cohorts involving 194,095 participants with a median follow-up of 8 years to explore the impact of different beverages on kidney stone formation. They reported a relationship between orange juice intake and a 12% reduction in kidney stone formation ($P = 0.004$). One limitation is that the association between drinks and various compositions of stones was not explored given little data available on urine compositions of participants. The included population was mostly of a white racial background, thereby limiting the application of results on other groups.

A randomized trial published in 2021 recruited 203 patients with recurrent calcium oxalate stones.[23] The team investigated the duration of stone recurrence over a 2-year period following supplementation with 60 mL lemon juice every 12 hours versus no supplementation. After 2 years, the recurrence rate of kidney stones was 31% in the control group and 21% in the intervention group ($P = 0.089$). They also noticed a reduction in urinary sodium excretion of 8.60 ± 65.68 mEq/day in the intervention group after 6 months. However, the treatment effect reduced progressively due to a decline in the adherence to lemon juice supplementation.

A retrospective study published in 2007 investigated the effect of lemonade on urine citrate and volume using 9-year data of 100 adults with recurrent calcium oxalate stones.[24] The first

Table 1: Recommended daily fluid intake with respect to age

Age group	Recommended water intake (ml/day)	Gender
0–6 mo	100–190 ml/kg/day from milk	Both
6–12 mo	800–1000 ml/day from milk	
2 y	1100–1200	
2–3 y	1300	
4–8 y	1600	
9–13 y	2100	Boys
9–13 y	1900	Girls
≥14 years old	2500	Boys
	2000	Women
Pregnant women	add 300 ml/day above the recommended	
Lactating women	add 700 ml/day above the recommended	

group (n = 63) received lemonade therapy only, whereas the second group (n = 37) received potassium citrate with lemonade therapy. Although lemonade therapy increased urinary citrate levels in both groups (203 mg/day in the first group and 346 mg/day in the second group), the increase from baseline to the last visit was significant in the second group only ($P = 0.008$). The maximum urine volume was higher in the second group than in the first group (860 mL/day vs 763 mL/day), but the increase was significant in both groups ($P < 0.001$).

In addition, a prospective study published in 2019 compared dietary lemonade and regular lemonade and their effects on kidney stone formation. Participants (n = 12) consumed 2 L of either regular lemonade (n = 6) or dietary lemonade (n = 6) alongside an oxalate- and sodium-controlled diet, and a 24-hour urine analysis was performed at baseline and on days 4 and 5. During the first 24 hours, urine volume increased from a baseline of 1.9 L to 2.6 L ($P = 0.006$) and 2.8 L ($P = 0.002$) among those who consumed regular and dietary lemonade, respectively, measured as mean value per day. On that test day, those who consumed dietary lemonade had a greater increase in urinary citrate from the baseline (an increase of 104 mg, $p = 0.041$) than those who consumed regular lemonade (a decrease of 76 mg, $P = 0.041$). A mean value determined after days 4 and 5 showed a significant reduction of supersaturation of calcium oxalate with dietary lemonade only (4.1 at baseline to 2.7 after dietary lemonade, $P = 0.006$).[25] The study was done as a short-term evaluation of a small group of healthy participants, thereby evaluating the immediate physiology without noting the effect of metabolic derangements.

Other fruit juices have also been studied to identify their effects on urinary oxalate, citrate, and pH, with varying results. An interventional study in which 12 healthy individuals were administered blackcurrant juice (330 mL/day) reported an increase in both urinary pH and urinary citrate levels, with a concomitant increase in urinary oxalate level.[26] Recently, a review of 13 articles found that grapefruit juice was protective against renal stones in small clinical studies but increased the risk of kidney stone disease in epidemiological studies.[27]

Soft drinks and carbohydrates

Fructose consumption is thought to affect calcium and oxalate excretion, as well as urine pH, increasing the risk of stone formation.[9] Previous research has shown that high consumption of simple carbohydrates, such as glucose or xylitol, can cause hypercalciuria and increase the risk of kidney stone disease.[28]

Pietro Ferraro *et al.*[22] found a 23% higher risk of renal stone formation in individuals consuming ≥1 sugar-sweetened cola serving per day than in those consuming <1 serving per week. They also reported a 33% increase in the risk of kidney stone formation with sugar-sweetened noncola drinks ($P = 0.003$) but a borderline risk of stone formation with artificially sweetened noncola drinks ($P = 0.05$). This trend was attributed to increased fructose content, supported by a marginal relationship between the consumption of artificially sweetened cola and kidney stone formation. Another study tested Sunkist orange soda diet and found no clinically significant changes in urine chemistry parameters related to calcium or uric stones.[29] Similarly, a recent interventional study did not find any significant relationship between the intake of carbonated drinks and kidney stone formation.[30] The effect of consuming soft drinks, such as Coca-Cola, which contain phosphoric acid, on the formation of struvite stones has also been investigated in a laboratory-based study.[31] The presence of a urinary tract infection with urease-positive bacteria and the availability of phosphoric acid provided a conducive environment for the formation of struvite stones.

Tea and coffee

A prospective cohort study with a remarkable population of 439,072 found that both tea (hazard ratio per 20 ml/day 0.95, 95% CI 0.92–0.99) and coffee (hazard ratio per 200 ml/day 0.92, 95% CI 0.88–0.95) had protective effects against renal stone formation.[32] Pietro Ferraro *et al.*[22] found a lower risk of kidney stone disease with consumption of tea (11%, $P = 0.02$), coffee (26%, $P < 0.001$), and decaffeinated coffee (16%, $P = 0.01$). Additionally, a recent systematic review found that caffeinated drinks have a hypercalciuric effect that is balanced by their diuretic effects. Green tea has been suggested to play a protective role against kidney stone formation.[33] No distinct comparisons were made between different caffeinated drinks in these studies. Although the oxalate content in coffee is low, it varies between black and green teas depending on the preparation process.[34] Thus, the protective mechanisms of black and green teas remain unclear. A recent case-control study published in 2021 found a significant association between increased consumption of tea and calcium oxalate stone formation but did not find this association with coffee.[35] They partly attributed this explanation to the lower consumption of coffee than of tea in their selected population. In another study, the association between recurrent renal stones and caffeine from both coffee and noncoffee sources was investigated.[36] Caffeine from coffee sources had an odds ratio of 1.13 (0.99–1.29) compared to an odds ratio of 0.90 (0.79–1.03) for noncoffee sources, with a linear relationship to stone formation regardless of the source of caffeine.

Interestingly, a systematic review and meta-analysis published in 2022 involving seven studies found that caffeine had a protective role against stone formation, with a relative risk of 0.68, 95% CI 0.61–0.75.[37] Moreover, a 2022 case-control study of 834 individuals in China found that drinking ≥180 mL tea daily had a protective role against hospitalization with kidney stone disease.[38] Green tea was found to be more protective (adjusted odds ratio of 0.189, $P < 0.001$) than black tea (adjusted odds ratio of 1.248, $P = 0.654$). This correlates with the finding of a 2021 study in a Chinese population that found an inverse association between tea and stone formation, with a linear trend.[39]

Compared with participants who did not consume tea (hazard ratio of 1.00), those who drank ≥7 cups of tea had a hazard ratio of 0.73 (95% CI 0.65–0.83) with $P < 0.001$.

A group of 10 previously healthy men participated in a two-phase study (5 days control with 1.5 L/day of fruit tea containing 0 mg black tea followed by 5 days of intervention with 1.5 L/day of 86 mg black tea). The two groups showed no significant difference in urinary oxalate excretion over 24 hours, but the intervention group had an increase in urine citrate content.[40]

Sodium chloride

Sodium chloride is one of the elements that influence the urinary risk profile for kidney stone formation.[9] The recommended daily intake for sodium is approximately 100 mmol (2300 mg) or 6 g of salt (sodium chloride).[41] Dietary sodium increases urinary calcium excretion, thus increasing the risk of kidney stone formation. Calcium reabsorption in the renal tubules is hindered by the expansion of the extracellular fluid volume as an effect of sodium.[9]

An interventional study conducted in 2020 explored the correlation between high sodium intake and calcium homeostasis to determine their effects on renal stone formation. The 24-hour urinary sodium and calcium excretions of 18 participants were analyzed after taking two different diets, including a sodium-restricted diet (RES) and a liberalized-sodium diet (LIB). Unlike RES diet, the LIB-diet suppressed renin activity ($P < 0.001$) and plasma aldosterone ($P < 0.001$) but increased calciuria ($P < 0.0001$) and decreased serum calcium ($P < 0.0001$).

The study concluded that an increase in the dietary intake of sodium chloride led to volume expansion and suppression of the renin-angiotensin-aldosterone system, decreased serum calcium levels, and induced urinary calcium excretion. Hypercalciuria was associated with increased risk of renal stone formation.[42]

A retrospective cohort study conducted in 2017 analyzed the effects of low-sodium and low-calcium diets on urinary oxalate excretion in 169 patients with documented calcium oxalate stones. They found a strong correlation between the low-sodium and low-calcium diets and reduced 24-hour urinary calcium and sodium excretion ($P < 0.0001$). For patients who often develop calcium oxalate stones, a diet low in sodium and calcium led to a considerable decrease in urinary calcium excretion, but no change was noted in urine volume.[43]

Despite the correlation between a high-sodium diet and kidney stone formation, some researchers have found a relationship between hyponatremia and renal stone formation. A case-control study conducted in the United States involving 3.4 million patient records from 2016 to 2018 explored the relationship between serum sodium concentrations and kidney stone disease. The patients were stratified into three groups, and the odds ratios (95% CI) for kidney stone formation among those with prior, recent, and persistent hyponatremia were 0.93, 2.02, and 6.25, respectively. They concluded that chronic persistent hyponatremia is a significant risk factor for kidney stone disease.[44]

Urinary excretions of sodium and calcium are closely related. Therefore, reducing salt intake is the simplest way to reduce the risk of kidney stone formation. Limiting salt consumption is encouraged by the American Urological Association; however, low-income families who rely on cheap, processed food may find this to be impractical.[45]

Calcium

Calcium can be obtained from dairy or nondairy sources, with dairy products being an excellent source.[46] Calcium phosphate and oxalate play important roles in the formation of kidney stones.[47] It may be assumed that reducing calcium intake through diet is a suitable treatment approach for kidney stone disease. However, compared to higher dietary intake, lower calcium intake was linked to an increased risk of kidney stone formation by over 50%.[48,49] Similarly, a randomized trial compared a low-calcium diet (400 mg/day) with a normal-calcium (1200 mg/day), low-salt, and low-animal protein diet in 120 men with recurring calcium oxalate stones.[50] After 5 years, the normal-calcium diet group showed a significant reduction in the incidence of stone recurrence by approximately 50%. Thus, balanced calcium intake from food appears to have a protective effect on kidney stone occurrence compared to low-calcium dietary intake.[46–49,51]

However, the relationship between the risk of kidney stones and calcium supplementation remains controversial.[47,49] In a 2006 study, 36,282 postmenopausal women were administered either 1000 mg/day of elemental calcium or a placebo and followed up for 7 years. A 17% increased risk of stone formation was found, with 449 women reporting kidney stones in the group receiving calcium with vitamin D compared with 381 women in the placebo group.[52] Of note, approximately 66.67% of participants in the intervention group who received supplements had minimal oxalate intake, suggesting that the duration of supplementation may have influenced this finding.[46,47,49,51] A prospective study of 8 years involving 96,245 women in the Nurses' Health Study II also found a reduction in the risk of kidney stone formation with increased dietary calcium intake ($P = 0.007$), but calcium supplementation was not associated with increased risk of stone formation.[53]

Domrongkitchaiporn *et al.*[54] conducted a randomized crossover study involving 32 healthy volunteers who consumed 1000 mg of calcium carbonate three times daily during meals or 3000 mg at bedtime to elucidate the contradictory role of calcium supplementation. Urinary calcium excretion increased considerably with both bedtime and calcium supplementation ($P < 0.05$), with no significant difference between the groups. However, taking calcium supplements at mealtimes resulted in lower urine oxalate excretion compared to baseline ($P = 0.01$). Of note, no difference was found in the urinary oxalate concentrations after bedtime calcium supplementation ($P = 0.9$).[54]

Oxalate

Hyperoxaluria (urinary oxalate excretion > 0.5 mmol/1.73 m^2/d) is one of the major risk factors for calcium oxalate stone formation.[55] Primary hyperoxaluria is attributed to inborn errors in the glyoxylate cycle, whereas secondary hyperoxaluria is due to either increased ingestion of oxalate (or its precursors, such as ascorbic acid) or increased enteric absorption.[56]

In the gastrointestinal tract, calcium binds to oxalate, thus limiting the amount of oxalate absorbed. A low-calcium diet increases oxalate absorption and its contribution to nephrolithiasis.[20] Moreover, an increase in oxalate availability for enteric absorption is related to fat malabsorption and calcium saponification.[57] A 2021 case-control study involved 430 volunteers found that dietary acid load increased the risk of calcium oxalate stone formation by an odds ratios of 1.43 for patients with newly diagnosed calcium oxalate stones and 1.88 for the control group, regardless of protein or potassium concentrations.[58]

The ingestion of foods with high oxalate bioavailability, such as chocolate and cola, contributes to hyperoxaluria.[59] In a 2005 interventional study exploring the relationship between plasma and urinary oxalate concentrations secondary to oral oxalate loading in a controlled dietary environment, Holmes *et al.*[60] found a transient increase in serum oxalate concentrations and renal secretion of oxalate. A strong correlation ($r = 0.43$, $P < 0.001$) was found between the ratio of oxalate-to-creatinine clearance and plasma oxalate level, without evidence of acute renal injury after 8 mmol oxalate load.[60]

Another study with a similar design compared urinary oxalate concentrations and the ratio of oxalate-to-creatinine clearance between six healthy individuals and six volunteers with a history of renal stones.[61] Urinary oxalate time and dose-dependent changes were found based on loading doses; however, no variation in oxalate excretion was observed between the two groups ($P = 0.96$ for urinary oxalate excretion and $P = 0.34$ for oxalate-to-creatinine clearance). The authors concluded that acute transient exposure might not be directly harmful.

In a study comparing the oxalate content of different fruits and vegetables, rhubarb nectar and beetroot juices showed the highest oxalate concentrations (198.3 mg/100 mL and 60.1–70.0 mg/100 mL, respectively).[62] A previous study identified common foods with high oxalate content such as rhubarb, spinach, and others, as shown in Table 2.[63] Nonetheless, a systematic review and meta-analysis found that, despite an increase in oxalate excretion from fruits and vegetables, a diet

Table 2: Oxalate content of different foods

Foodstuff	Oxalate (mg/100g FW) Range	Mean
Group 1		
Rhubarb (Rheum rhaponticum) Victoria, forced, stewed raw	260 275–1336	805
Red beetroot (Beta vulgaris)	121–450	275
Common sorrel (Rumex acetosa)	270–730	500
Garden sorrel (Rumex patientia)	300–700	500
Pig spinach (Chenopodium spp.)	1100	
Purslane (Portulaca oleracea)	910–1679	1294
Spinach (Spinacia oleracea)	320–1260	970
Garden orach (Atriplex hortensis)	300–1500	900
NZ spinach (Tetragonia expansa)	890	
Coffee (Coffea arabica)	50–150	100
Cashew (Anacardium occidentale)	231	
Cocoa (Theobroma cacao)	500–900	700
Beet leaves (Beta vulgaris var. cicla)	300–920	610
Rhubarb (Rheum rhaponticum) Crimson, end of season, stewed	460	
Group 2		
Potato (Solanum tuberosum)	20–141	80
Amaranth (Amaranthus polygonoides)	1586	
Tea (Thea chinensis)	300–2000	1150
Amaranth (Amaranthus tricolor)	1087	
Rhubarb (Rheum rhaponticum) Victoria, end of season, stewed	620	
Group 3		
Apple (Malus spp.)	0–30	15
Blackcurrant (Ribes nigrum)	2–90	50
Tomato (Lycopersicon esculentum)	5–35	20
Parsley (Petroselinum sativum)	140–200	170
Cabbage (Brassica oleracea)	0–125	60
Lettuce (Lactuca sativa)	5–20	12

Ratio of oxalate in various typical foods (mg/100g, fresh weight [FW]). Depending on their oxalate ratio, these foods have been separated into three major groups. Group 1, > 2.0; Group 2, 1.0-2.0; and Group 3, 1.0

high in fiber, vegetables, and fruits with reduced animal proteins was recommended.[13] However, fruits and vegetables have been observed to increase urinary pH (from 5.84 to 6.19) as well as the volume by 64%, while promoting the excretion of protective citrate, potassium, and magnesium ($P < 0.05$).[64]

Proteins

Adults should consume 0.8–1.0 g protein/kg of normal body weight per day.[9] A 2022 systematic review and meta-analysis involving 14 prospective cohort studies explored the relationship between the risk of kidney stone disease in the general population and proteins from different sources (dairy proteins, nondairy animal proteins, meat products, and processed meat).[65] Nondairy animal protein, meat products, and processed meat were all associated with a higher risk of kidney stones, with (RR: 1.11; 95% CI: 1.03, 1.20; I2 = 0%, n = 4), (RR: 1.22; 95% CI: 1.09, 1.38; I2 = 13%, n = 3), and (RR: 1.29; 95% CI: 1.10, 1.51; I2 = 0%, n = 2), respectively.[65]

Dairy protein and kidney stone disease showed an inverse association (RR: 0.91; 95% CI: 0.84, 0.99; I2 = 0%, n = 4). Additionally, consumption of red meat was substantially linked to an increased risk of kidney stones for every 100 g consumed (relative risk: 1.39; 95% CI 1.13–1.71).[65] However, Egger's and Begg's tests revealed a publication bias regarding the association between dietary animal proteins and renal stones. According to the NutriGrade scoring system[66] used by the researchers, the credibility of the evidence was low.[65]

The relationship between plant proteins and incidence of kidney stones has been investigated.[67] Plant protein concentrations were not associated with the incidence of kidney stone formation ($p$trend = 0.14). Of note, plant protein sources, such as soybeans and lentils, have a protective risk against renal stone formation when plant protein is consumed in proportion to animal protein.[67]

To understand how proteins interact with the surface of calcium oxalate crystals and their role in stone formation or inhibition, it is crucial to consider their polymeric nature. Polymer accumulation is reported to play a significant role in inhibiting the growth of calcium oxalate crystals and the promotion of crystal aggregation, which does not rely on different protein conformations (secondary or tertiary structures).[68] Recent research has revealed that stone matrices contain hundreds of proteins with no clear reason for their inclusion.[69] Several studies have attempted to explain the effects of proteins on crystal growth. Additionally, the mechanisms by which these proteins affect the development of calcium oxalate kidney stones have been examined.[69,70] Consumption of protein supplements also influences kidney stone formation. An interventional study conducted in 2017 observed 18 healthy adults after 3 days of consuming whey protein or albumin supplements in habitual amounts (one scoop per day) while maintaining regular protein consumption. The researchers found no alterations in the median values of lithogenic urine parameters from baseline (urine sodium, calcium, oxalate, citrate, phosphorus, magnesium, urate, potassium, creatinine, or pH). However, they showed an increase in the mean protein equivalent of nitrogen appearance ($P < 0.001$).[71]

At an individual level, following whey protein or albumin supplementation, 39% of participants showed a more than 50% increase in urine calcium excretion and a varied decrease in urinary pH (44% of participants after whey protein supplementation and 67% after albumin supplementation). One-third of patients experienced an increase of more than 50% in urine salt content following albumin supplementation. This study cautions against the use of such supplements by kidney stone formers, and in addition to customized dietary recommendations, it indicates the need for concurrent tighter surveillance of urine calcium, salt, pH, and other urinary parameters.[71]

Fats

The relationship between dietary fatty acid composition and urinary oxalate excretion was investigated by analyzing 24-hour urine samples collected from 58 participants with a history of renal stones. An association between arachidonic acid (prominent in animal proteins) and increased urinary oxalate excretion was observed ($P = 0.003$).[72]

The role of fish oil supplementation in the dietary control of stone formation has been the subject of several studies. A literature review published in 2021 found that in most trials, fish oil supplementation reduced urine excretion of calcium and oxalate in both healthy candidates and stone formers.[9] One of these trials studied 15 healthy individuals for 30 days. They followed a standardized diet in addition to taking fatty acid supplements daily. The study showed a significant decrease in oxalate stone formation by 23% (p 0.023).[9] A 2020 review analyzes 16 various study designs that addressed the concern of dietary polyunsaturated fatty acids' (PUFAs) potential significance in regulating the production of stones. It showed that PUFAs may have protective effects against calcium oxalate renal stones.[73]

Obesity is strongly associated with kidney stone formation.[74] The likelihood of developing acute kidney stones is strongly correlated with the body mass index (BMI), waist circumference, and weight. BMI was considerably higher in stone-forming individuals and may be linked to the development of several forms of urinary stones. A raised BMI is linked to a 1.30-fold greater risk of incident kidney stones compared to women with a BMI in the normal range, according to multivariate analysis of a research including 84,225 postmenopausal women.[74]

A 2022 study conducted in Korea involving 28,395 kidney stone patients and 113,580 healthy controls found a link between BMI and nephrolithiasis.[75] The odds ratio (95% CI) for being overweight (BMI 25.0 to <30) was 1.27 (1.22–1.3), that for obese I (BMI 30 to <35) was <1.42 (1.37–1.46), and that for obese

II (BMI 35 to <40) was <1.59 (1.47–1.71). A cross-sectional analysis published in 2021 with 13,223 participants found a positive nonlinear relationship between an increase in BMI and nephrolithiasis ($P < 0.001$).[76]

A study conducted in a US adult population of 10,271 participants (>40 years of age) confirmed an association between visceral fat and renal stone disease. Total and truncal fat factors were linked to a greater prevalence of renal stones. In males, higher fat percentage was associated with higher odds of kidney stones [per 5% total fat: odds ratio (OR) =1.19, 95% confidence interval (CI) 1.08–1.32; per 5% truncal fat: OR = 1.22, 95% CI 1.10–1.35]. In females, higher fat percentage was associated with higher odds of kidney stones overall (per 5% total fat: OR = 1.23, 95% CI 1.10–1.37; per 5% truncal fat: OR = 1.20, 95% CI 1.08–1.33).[77]

Increased vesicular fat mass is associated with renal stone formation and may contribute to stone recurrence. Compared to patients who developed kidney stones for the first time, those with a history of stones had a higher visceral fat ratio with a *P* value of 0.03 based on a study that was done on 148 patients.[78]

Pediatric patients with epilepsy have been known to benefit from ketogenic diets; nevertheless, adults have been using them more frequently recently for weight loss purposes.[79] A 2021 systematic review and meta-analysis of 36 studies found a total incidence of kidney stones of 5.9% among 2795 participants following a ketogenic diet, with 7.9% in adults and 5.8% in children. Common types included 48.7% uric acid, 36.5% calcium oxalate, and 27.8% mixed stones.[79]

Conclusion

Nutrition plays an essential role in the management and prevention of kidney stones. In this review, we investigated the influence of dietary habits on the risk of nephrolithiasis. We found that sufficient fluid intake and low-salt diets have a protective role against nephrolithiasis. Fruit juices, particularly those that increase urinary citrate concentrations, such as lemonade and grapefruit juice, can have protective effects against stone formation. Meanwhile, carbonated drinks did not increase the risk of nephrolithiasis; however, the addition of fructose increased this risk.

Although the findings of some studies on tea and caffeine consumption were inconclusive and contradictory, the majority seem to suggest that tea, particularly green tea, plays the most protective role against nephrolithiasis. However, it remains unclear whether coffee, as opposed to caffeine, promotes renal stone formation.

Studies on the relationship between the different proteins and stone formation revealed that red meat was the most important factor. Plant-based proteins have been found to contribute to nephrolithiasis but to a lesser extent than animal-sourced proteins. Regarding oxalate consumption, researchers found that shorter exposure did not pose a greater risk compared to prolonged exposure to foods with high oxalate bioavailability. Nonetheless, researchers recommend a balanced diet with fiber-rich fruits and vegetables owing to the renoprotective roles of citrate and electrolytes, such as potassium and magnesium. A diet with balanced calcium amounts is more protective than calcium supplementation alone.

Nephrolithiasis is also associated with obesity. Whether this relationship is mainly due to the pathophysiology of obesity or due to the involvement of other factors, such as dietary habits of individuals with higher BMI, remains unclear. Further research on whether a change in the dietary habits of this population would alter the risk of kidney stone disease is warranted.

In conclusion, this review has supported the harmful effects of a high intake of sodium, certain fatty acids (notably arachidonic acid), oxalate, fructose, and animal proteins. A balanced diet composed of n-3 PUFAs, fish oils, calcium, and sufficient fluid intake plays a protective role in reducing the formation and recurrence of kidney stones. Moreover, The EAU Urolithiasis Guidelines recommend and emphasize several dietary and lifestyle modifications to reduce the risk of kidney stone formation and recurrence.

Adequate fluid intake, targeting a urine output of at least 2–3 liters per day, is recommended, with water being the preferred beverage choice. A low-sodium diet, with sodium intake limited to less than 2.3 g per day, is advised. Patients should moderate their intake of animal proteins, favoring plant-based protein sources. Incorporation of fiber-rich fruits and vegetables is encouraged to leverage the protective effects of citrate, potassium, and magnesium. Maintaining a balanced calcium intake, rather than relying solely on supplementation, may be more effective.

Achieving and sustaining a healthy body mass index is also important as obesity is associated with an increased risk of nephrolithiasis. Limiting consumption of carbonated beverages, especially those containing fructose, and potentially including green tea in the diet may also confer benefits. For high-risk patients, a comprehensive metabolic evaluation is recommended to identify individualized risk factors and guide personalized prevention strategies.[80]

Data availability

The data used to support the findings of this study are included within the article.

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Conflicts of interest

There are no conflicts of interest.

References

1. Romero V, Akpinar H, Assimos DG. Kidney stones: A global picture of prevalence, incidence, and associated risk factors. Rev Urol 2010;12:e86-96.
2. Ward JB, Feinstein L, Pierce C, Lim J, Abbott KC, Bavendam T, *et al.* Pediatric urinary stone disease in the United States: The Urologic Diseases in America Project. Urology 2019;129:180-7.
3. Dwyer ME, Krambeck AE, Bergstralh EJ, Milliner DS, Lieske JC, Rule AD. Temporal trends in incidence of kidney stones among children: A 25-year population based study. J Urol 2012;188:247-52.
4. Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. Renal stone epidemiology: A 25-year study in Rochester, Minnesota. Kidney Int 1979;16:624-31.
5. Miyake O, Yoshimura K, Tsujihata M, Yoshioka T, Koide T, Takahara S, *et al.* Possible causes for the low prevalence of pediatric urolithiasis. Urology 1999;53:1229-34.
6. Dhondup T, Kittanamongkolchai W, Vaughan LE, Mehta RA, Chhina JK, Enders FT, *et al.* Risk of ESRD and mortality in kidney and bladder stone formers. Am J Kidney Dis 2018;72:790-7.
7. Shoag J, Halpern J, Goldfarb DS, Eisner BH. Risk of chronic and end stage kidney disease in patients with nephrolithiasis. J Urol 2014;192:1440-5.
8. Lieske JC, Rule AD, Krambeck AE, Williams JC, Bergstralh EJ, Mehta RA, *et al.* Stone composition as a function of age and sex. Clin J Am Soc Nephrol 2014;9:2141-6.
9. Siener R. Nutrition and kidney stone disease. Nutrients 2021;13:1917.
10. Han H, Segal AM, Seifter JL, Dwyer JT. Nutritional management of kidney stones (nephrolithiasis). Clin Nutr Res 2015;4:137-52.
11. Lotan Y, Antonelli J, Jiménez IB, Gharbi H, Herring R, Beaver A, *et al.* The kidney stone and increased water intake trial in steel workers: Results from a pilot study. Urolithiasis 2017;45:177-83.
12. Atan L, Andreoni C, Ortiz V, Silva EK, Pitta R, Atan F, *et al.* High kidney stone risk in men working in steel industry at hot temperatures. Urology 2005;65:858-61.
13. Lin BB, Lin ME, Huang RH, Hong YK, Lin BL, He XJ. Dietary and lifestyle factors for primary prevention of nephrolithiasis: A systematic review and meta-analysis. BMC Nephrol 2020;21:267.
14. Cheungpasitporn W, Rossetti S, Friend K, Erickson SB, Lieske JC. Treatment effect, adherence, and safety of high fluid intake for the prevention of incident and recurrent kidney stones: A systematic review and meta-analysis. J Nephrol 2016;29:211-9.
15. Servais A, Thomas K, Dello Strologo L, Sayer JA, Bekri S, Bertholet-Thomas A, *et al.* Cystinuria: clinical practice recommendation. Kidney Int 2021;99:48-58.
16. Barbey F, Joly D, Rieu P, Méjean A, Daudon M, Jungers P. Medical treatment of cystinuria: Critical reappraisal of long-term results. J Urol 2000;163:1419-23.
17. Armstrong LE, Johnson EC. Water intake, water balance, and the elusive daily water requirement. Nutrients 2018;10:1928.
18. Agostoni C, Bresson JL, Fairweather-Tait S, Flynn A, Golly I, Korhonen H, *et al.* Scientific opinion on dietary reference values for water. EFSA J 2010;8:1459.
19. Viljoen A, Chaudhry R, Bycroft J. Renal stones. Ann Clin Biochem 2019;56:15-27.
20. Heilberg IP, Goldfarb DS. Optimum nutrition for kidney stone disease. Adv Chronic Kidney Dis 2013;20:165-74.
21. Hamm LL, Hering-Smith KS. Pathophysiology of hypocitraturic nephrolithiasis. Endocrinol Metab Clin North Am 2002;31:885-93.
22. Ferraro PM, Taylor EN, Gambaro G, Curhan GC. Soda and other beverages and the risk of kidney stones. Clin J Am Soc Nephrol 2013;8:1389-95.
23. Ruggenenti P, Caruso MR, Cortinovis M, Perna A, Peracchi T, Giuliano GA, *et al.* Fresh lemon juice supplementation for the prevention of recurrent stones in calcium oxalate nephrolithiasis: A pragmatic, prospective, randomised, open, blinded endpoint (PROBE) trial. EClinicalMedicine 2022;43:101227. doi: 10.1016/j.eclinm.2021.101227.
24. Penniston KL, Steele TH, Nakada SY. Lemonade therapy increases urinary citrate and urine volumes in patients with recurrent calcium oxalate stone formation. Urology 2007;70:856-60.
25. Cheng JW, Wagner H, Asplin JR, Hodgkin G, Schlaifer A, Fargusson M, *et al.* The effect of lemonade and diet lemonade upon urinary parameters affecting calcium urinary stone formation. J Endourol 2019;33:160-6.
26. Kessler T, Jansen B, Hesse A. Effect of blackcurrant-, cranberry- and plum juice consumption on risk factors associated with kidney stone formation. Eur J Clin Nutr 2002;56:1020-3.
27. Barghouthy Y, Somani BK. Role of citrus fruit juices in prevention of kidney stone disease (KSD): A narrative review. Nutrients 2021;13:4117.
28. Barghouthy Y, Corrales M, Somani B. The relationship between modern fad diets and kidney stone disease: A systematic review of literature. Nutrients 2021;13:4270.
29. Sumorok NT, Asplin JR, Eisner BH, Stoller ML, Goldfarb DS. Effect of diet orange soda on urinary lithogenicity. Urol Res 2012;40:237-41.
30. Adeel M, Zainab S, Athar S, Khoso A. Association of nephrolithiasis with the intake of carbonated drinks. Professional Med J 2021;28:592-7.
31. Skubisz M, Torzewska A, Mielniczek-Brzóska E, Prywer J. Consumption of soft drinks rich in phosphoric acid versus struvite crystallization from artificial urine. Sci Rep 2022;12:14332.
32. Littlejohns TJ, Neal NL, Bradbury KE, Heers H, Allen NE, Turney BW. Fluid intake and dietary factors and the risk of incident kidney stones in UK Biobank: A population-based prospective cohort study. Eur Urol Focus 2020;6:752-61.
33. Barghouthy Y, Corrales M, Doizi S, Somani BK, Traxer O. Tea and coffee consumption and pathophysiology related to kidney stone formation: A systematic review. World J Urol 2021;39:2417-26.
34. Siener R, Seidler A, Voss S, Hesse A. Oxalate content of beverages. J Food Compost Anal 2017;63:184-8.
35. Haghighatdoost F, Sadeghian R, Abbasi B. The associations between tea and coffee drinking and risk of calcium-oxalate renal stones. Plant Foods Hum Nutr 2021;76:516-22.
36. Sun Y, Wang D, Zhou Q. Caffeine intake and the risk of

recurrent kidney stones in adults, an analysis of 2007-2014 National Health and Nutrition Examination Surveys. Eur J Nutr 2020;59:2683-92.

37. Zhao J, Huang Y, Yu X. Caffeine intake and the risk of incident kidney stones: A systematic review and meta-analysis. Int Urol Nephrol 2022;54:2457-66.
38. Liu Y, Bi S, Li H, Shi J, Xia Y, Niu K, *et al.* Association between tea intake and hospitalized nephrolithiasis in Chinese adults: A case-control study. Front Nutr 2022;9:1014491.
39. Wang H, Fan J, Yu C, Guo Y, Pei P, Yang L, *et al.* Consumption of tea, alcohol, and fruits and risk of kidney stones: A prospective cohort study in 0.5 million Chinese adults. Nutrients 2021;13:1119.
40. Siener R, Hesse A. Effect of black tea consumption on urinary risk factors for kidney stone formation. Nutrients 2021;13:4434.
41. Pearle MS, Goldfarb DS, Assimos DG, Curhan G, Denu-Ciocca CJ, Matlaga BR, *et al.* Medical management of kidney stones: AUA guideline. J Urol 2014;192:316-24.
42. Bayomy O, Zaheer S, Williams JS, Curhan G, Vaidya A. Disentangling the relationships between the renin-angiotensin-aldosterone system, calcium physiology, and risk for kidney stones. J Clin Endocrinol Metab 2020;105:1937-46.
43. Seeger H, Kaelin A, Ferraro PM, Weber D, Jaeger P, Ambuehl P, *et al.* Changes in urinary risk profile after short-term low sodium and low calcium diet in recurrent Swiss kidney stone formers. BMC Nephrol 2017;18:349.
44. Tominaga N, Fernandez SJ, Mete M, Shara NM, Verbalis JG. Hyponatremia and the risk of kidney stones: A matched case-control study in a large U.S. health system. PLoS One 2018;13:e0203942.
45. Filler G, Salerno F, McIntyre CW, De Ferris MED. Animal, human, and 23NA MRI imaging evidence for the negative impact of high dietary salt in children. Curr Pediatr Rep 2021;9:110–117.
46. Cormick G, Belizán JM. Calcium intake and health. Nutrients 2019;11:1606.
47. Li K, Wang XF, Li DY, Chen YC, Zhao LJ, Liu XG, *et al.* The good, the bad, and the ugly of calcium supplementation: A review of calcium intake on human health. Clin Interv Aging 2018;13:2443-52.
48. Ferraro PM, Bargagli M, Trinchieri A, Gambaro G. Risk of kidney stones: Influence of dietary factors, dietary patterns, and vegetarian-vegan diets. Nutrients 2020;12:779.
49. Bargagli M, Ferraro PM, Vittori M, Lombardi G, Gambaro G, Somani B. Calcium and vitamin D supplementation and their association with kidney stone disease: A narrative review. Nutrients 2021;13:4363.
50. Borghi L, Schianchi T, Meschi T, Guerra A, Allegri F, Maggiore U, *et al.* Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. N Engl J Med 2002;346:77-84.
51. Ticinesi A, Nouvenne A, Chiussi G, Castaldo G, Guerra A, Meschi T. Calcium oxalate nephrolithiasis and gut microbiota: Not just a gut-kidney axis. A nutritional perspective. Nutrients 2020;12:548.
52. Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, *et al.* Calcium plus vitamin D supplementation and the risk of fractures. N Engl J Med 2006;354:669-83.
53. Curhan GC, Willett WC, Knight EL, Stampfer MJ. Dietary factors and the risk of incident kidney stones in younger women: Nurses' Health Study II. Arch Intern Med 2004;164:885-91.
54. Domrongkitchaiporn S, Sopassathit W, Stitchantrakul W, Prapaipanich S, Ingsathit A, Rajatanavin R. Schedule of taking calcium supplement and the risk of nephrolithiasis. Kidney Int 2004;65:1835-41.
55. Dill H, Martin-Higueras C, Hoppe B. Diet-related urine collections: Assistance in categorization of hyperoxaluria. Urolithiasis 2022;50:141-8.
56. Bhasin B, Ürekli HM, Atta MG. Primary and secondary hyperoxaluria: Understanding the enigma. World J Nephrol 2015;4:235-44.
57. Witting C, Langman CB, Assimos D, Baum MA, Kausz A, Milliner D, *et al.* Pathophysiology and treatment of enteric hyperoxaluria. Clin J Am Soc Nephrol. 2021;16:487-95.
58. Haghighatdoost F, Sadeghian R, Clark CC, Abbasi B. Higher dietary acid load is associated with an increased risk of calcium oxalate kidney stones. J Ren Nutr 2021;31:467–74.
59. Prezioso D, Strazzullo P, Lotti T, Bianchi G, Borghi L, Caione P, *et al.* Dietary treatment of urinary risk factors for renal stone formation. A review of CLU Working Group. Arch Ital Urol Androl 2015;87:105-20.
60. Holmes RP, Ambrosius WT, Assimos DG. Dietary oxalate loads and renal oxalate handling. J Urol 2005;174:943-7; discussion 947.
61. Knight J, Holmes RP, Assimos DG. Intestinal and renal handling of oxalate loads in normal individuals and stone formers. Urol Res 2007;35:111-7.
62. Siener R, Seidler A, Voss S, Hesse A. The oxalate content of fruit and vegetable juices, nectars and drinks. J Food Compost Anal 2016;45:108-12.
63. Noonan SC, Savage GP. Oxalate content of foods and its effect on humans. Asia Pac J Clin Nutr 1999;8:64-74.
64. Meschi T, Maggiore U, Fiaccadori E, Schianchi T, Bosi S, Adorni G, *et al.* The effect of fruits and vegetables on urinary stone risk factors. Kidney Int 2004;66:2402-10.
65. Asoudeh F, Talebi S, Jayedi A, Marx W, Najafi MT, Mohammadi H. Associations of total protein or animal protein intake and animal protein sources with risk of kidney stones: A systematic review and dose-response meta-analysis. Adv Nutr 2022;13:821-32.
66. Schwingshackl L, Knüppel S, Schwedhelm C, Hoffmann C, Missbach G, Stelmach-Mardas B, *et al.* Perspective: NutriGrade: A scoring system to assess and judge the meta-evidence of randomized controlled trials and cohort studies in nutrition research. Adv Nutr 2016;7:994-1004.
67. Shu X, Calvert JK, Cai H, Xiang YB, Li H, Zheng W, *et al.* Plant and animal protein intake and risk of incident kidney stones: Results from the Shanghai men's and women's health studies. J Urol 2019;202:1217-23.
68. Rimer JD, Kolbach-Mandel AM, Ward MD, Wesson JA. The role of macromolecules in the formation of kidney stones. Urolithiasis 2017;45:57-74.
69. Berger GK, Eisenhauer J, Vallejos A, Hoffmann B, Wesson JA. Exploring mechanisms of protein influence on calcium oxalate kidney stone formation. Urolithiasis 2021;49:281-90.
70. Tanaka Y, Maruyama M, Okada A, Furukawa Y, Momma K, Sugiura Y, *et al.* Multicolor imaging of calcium-binding proteins in human kidney stones for elucidating the effects of proteins on crystal growth. Sci Rep

2021;11:16841.

71. Hattori CM, Tiselius HG, Heilberg IP. Whey protein and albumin effects upon urinary risk factors for stone formation. Urolithiasis 2017;45:421-8.
72. Naya Y, Ito H, Masai M, Yamaguchi K. Association of dietary fatty acids with urinary oxalate excretion in calcium oxalate stone-formers in their fourth decade. BJU Int 2002;89:842-6.
73. Rodgers AL, Siener R. The efficacy of polyunsaturated fatty acids as protectors against calcium oxalate renal stone formation: A review. Nutrients 2020;12:1069.
74. Poore W, Boyd CJ, Singh NP, Wood K, Gower B, Assimos DG. Obesity and its impact on kidney stone formation. Rev Urol 2020;22:17-23.
75. Kim SY, Yoo DM, Bang WJ, Choi HG. Obesity is positively associated and alcohol intake is negatively associated with nephrolithiasis. Nutrients 2022;14:4122.
76. Feng X, Wu W, Zhao F, Xu F, Han D, Guo X, *et al*. Relationship between body mass index and kidney stones based on dose-response analyses using restricted cubic splines applied to NHANES 2011-2016 data. J Ren Nutr 2021;31:263-9.
77. Abufaraj M, Siyam A, Xu T, Imm K, Cao C, Waldoer T, *et al*. Association between body fat mass and kidney stones in US adults: Analysis of the national health and nutrition examination survey 2011-2018. Eur Urol Focus 2022;8:580-7.
78. Yamashita S, Iguchi T, Nishizawa S, Iba A, Kohjimoto Y, Hara I. Recurrent stone-forming patients have high visceral fat ratio based on computed tomography images compared to first-time stone-forming patients. Int J Urol 2018;25:569-73.
79. Acharya P, Acharya C, Thongprayoon C, Hansrivijit P, Kanduri SR, Kovvuru K, *et al*. Incidence and characteristics of kidney stones in patients on ketogenic diet: A systematic review and meta-analysis. Diseases 2021;9:39.
80. EAU guidelines on urolithiasis-Guidelines. (2024, April). Uroweb-European Association of Urology. Available from: https://uroweb.org/guidelines/urolithiasis/chapter/guidelines.