SCRIPTA SCORE Scientific Medical Journal Vol. 6 No. 1 (2024) 28-37

talenta PUBLISHER

SCRIPTA SCORE Scientific Medical Journal
Journal homepage: https://talenta.usu.ac.id/scripta

Low Oxalate Diet for Prevention of Kidney Stone Disease: A Literature Review

Mochammad Haikal Alhamdi*[1], Ghina Jilan Alimah[1]
[1]*Department of Surgery, Faculty of Medicine, University of Jenderal Soedirman, Banyumas, Indonesia, 53146*
*Corresponding Author: mochhaikal17@gmail.com

ARTICLE INFO

Article history:
Received 29 March 2024
Revised 7 May 2024
Accepted 28 June 2024
Available online 15 August 2024

E-ISSN: 2686-0864
P-ISSN: 2088-8686

How to cite:
Alhamdi MH, Alimah GJ. Low Oxalate Diet for Prevention of Kidney Stone Disease: A Literature Review. SCRIPTA SCORE Sci Med J. 2024 Aug 15; 6(1):28-37

https://doi.org/10.32734/scripta.v6i1.16080

ABSTRACT

Background: Nephrolithiasis is the most common illness affecting the urinary system. It affects 600,000 Americans annually and about 12% of the world's population. It caused by a concentration of crystals that exits the kidney and genitourinary system. Calcium stones, primarily composed of calcium phosphate or oxalate, are present in about 80% of patients with nephrolithiasis. Kidney stones can be avoided by controlling the production of oxalate stones through the low oxalate dietary sources and regulating other factors that affect oxalate absorption. **Objectives:** The purpose of this literature review is to explain how to maintain a low-oxalate diet and other factors, such as enzymes, oxalate precursors, and bacteria in the colon, affect urine oxalate excretion and help prevent the formation of kidney stones. **Methods:** A summary of this literature was compiled using data from numerous journal databases, such as NCBI, Google Scholar, Science Direct, Elsevier, Springer Nature, Wiley Online Library, World Health Organization. Ten earlier research RCTs with statistical analysis—that met a number of inclusion criteria were used to support the goals of this work using PICO analysis. **Discussion:** Consuming more water, DASH, low calcium and salt diet, and low-oxalate diet can considerably reduce the excretion of oxalate. Conversely, a poor dietary pattern has been associated with an increased risk of kidney stones. Oral formulations ALLN-177, Oxabact, and OxDC are helpful in lowering urinary oxalate levels. **Conclusion:** Kidney stone disease may be avoided by adopting a low-oxalate and low-precursor diet.
Keyword: Hyperoxaluria, Kidney Stones, Oxalate, Oxalate Dietary, Oxalate Precursors

ABSTRAK

Latar Belakang: Nefrolitiasis merupakan penyakit yang banyak terjadi pada sistem saluran kemih. Penyakit ini mempengaruhi 600.000 orang Amerika setiap tahunnya dan sekitar 12% populasi dunia. Hal ini disebabkan oleh peningkatan konsentrasi kristal di sistem genitourinari. Pada pasien nefrolitiasis, 80% diantaranya disebabkan oleh pembentukan batu kalsium, terutama fosfat atau oksalat. Nefrolitiasis dapat dihindari dengan mengendalikan produksi batu oksalat melalui sumber makanan rendah oksalat dan mengatur faktor lain yang mempengaruhi penyerapan oksalat. **Tujuan:** Penulisan literatur ditujukan untuk mengetahui pengaturan pola makan rendah oksalat dan faktor lain seperti enzim, prekursor oksalat dan bakteri di usus sebagai pencegahan pembentukan batu oksalat di ginjal dengan menurunkan eksresi oksalat dalam urin. **Metode:** Literature review dilakukan dengan mengumpulkan berbagai literatur bersumber dari database jurnal, seperti NCBI, Google Scholar, Science Direct, Elsevier, Springer Nature, Wiley Online Library, World Health Organization. Digunakan 10 penelitian RCT yang sesuai dengan kriteria inklusi dengan analisis PICO. **Diskusi:** Peningkatan konsumsi air, DASH, diet rendah kalsium dan rendah garam dapat menurunkan eksresi oksalat. Pola diet yang buruk dapat meningkatkan risiko pembentukan batu ginjal. Konsumsi ALLN-177, Oxabact dan OxDC membantu menurunkan oksalat urin. **Kesimpulan:** Pembentukan batu ginjal dapat dihindari dengan menerapkan pola makan rendah oksalat dan rendah prekursor oksalat
Kata Kunci: Batu Ginjal, Oksalat, Pola Makan Oksalat, Prekursor Oksalat

1. Introduction

The most prevalent disorder affecting the urinary system is nephrolithiasis, also known as kidney stones. It affects around 12% of the global population and affects 600,000 Americans annually. It arises from a crystal or crystalline concretion that passes through the genitourinary system after leaving the kidney.[1] An increased risk of end-stage renal failure, cardiovascular disease, diabetes, hypertension, and kidney stones is associated with kidney stones.[2]

About 80% of nephrolithiasis patients have calcium stones, the majority of which are mostly made of calcium phosphate or calcium oxalate. The other common kinds include cystine stones, struvite (magnesium ammonium phosphate), and uric acid. Phosphorous chemical alterations and supersaturation of urine are involved in the production of renal stones. Nucleation and crystal concretions occur when solutes precipitate in urine under supersaturation conditions. How a liquid turns into a solid is dependent on the pH and certain excess ingredient amounts. Crystallization in nephrolithiasis is associated with supersaturation of stone-forming substances such as phosphorus, calcium, uric acid, oxalate, cystine, and low urine volume. By preventing supersaturation, nephrolithiasis can be avoided.[3]

Most stones are mostly composed of calcium oxalate. Usually, they come with hypercalciuria, hyperoxaluria, hypomagnesuria, hyper cystinuria, and hypocitraturia. Based on the etiology and severity of the clinical presentation, the causes of excess urine oxalate, or hyperoxaluria, can be divided into primary and secondary categories.[4] Oxalate is the single most potent urine molecule that promotes renal calculi. When urine oxalate levels rise from 20 mg to 40 mg per day, kidney stone risk increases by 2.5 to 3.5 times. Kidney stone formation can be greatly impacted by even relatively little variations in urine oxalate.[5] This review aims to discuss the kidney stones, oxalate metabolism, and how low diet oxalate affects process of kidney stone formation.

2. Method

This study is a literature review which is a methodological approach used to organize and analyse relevant literatures systematically. This literature review analysis was synthesized using PICO analysis and obtained from various online journal databases such as NCBI, Google Scholar, Science Direct, Elsevier, Springer Nature, Wiley Online Library, World Health Organization. The keywords used in the literature searching were oxalate dietary, precursors oxalate, kidney stone formation. Scientific articles were selected based on the following inclusion criteria: (1) Randomized controlled trial studies with statistical analysis, (2) The journal can be freely accessed, (3) Publication year of journal is not less than 2014, and (4) Matched with the material discussed in this literature review. All selected literature is analysed and the material is combined into a logical flow of ideas.

3. Discussion

3.1 Kidney Stones Disease

Kidney stones, also called renal calculi, are crystal concretions that usually occur in the kidney and are referred to as nephrolithiasis. About 12% of people worldwide suffer from nephrolithiasis, a condition with rising prevalence and recurrence rates and few effective treatment choices.[1] Kidney stones is influenced by certain diseases, habits, and composition of urine such as personal history of prior kidney stones, family history of kidney stones, increased enteric absorption of oxalate due to malabsorption, urinary tract infections, low fluid intake, history of certain metabolic diseases (diabetes, obesity, and hypertension), and acidic urine.[6]

Renal function can be evaluated in the lab using several assays, such as a basic or full metabolic panel. Urine pH, electrolytes, and urinalysis results can also assist identify a particular kind of stone. Another alternative is a KUB (kidney-ureter-bladder) X-ray, although this imaging method has limitations when it comes to uric acid stone detection. It is also possible to perform a more sensitive CT scan of the abdomen and pelvis without the use of contrast. When a kidney stone is suspected, contrast medium is usually avoided because it can mask stone results by enhancing the arteries and ureters.[2]

Treatment for nephrolithiasis is combined with conservative, pharmaceutical, and surgical approaches in the management of a patient with hyperoxaluria.[7] Treatment options for isolated renal stones include conservative measures such as fluids and alpha-blockers, as well as surgical procedures if the stone(s) is/are large, does not pass, or an infection complicates the situation.[8] Increased fluid consumption will result in more urine and less calcium oxalate supersaturation. It is advised that the oral intake be adequate to produce 2,000 ml of urine per day or more.[9] Dietary adjustments have shown beneficial and simple to implement in cases with secondary

hyperoxaluria. Eat less of the following foods high in oxalate: tea, dark-leafed vegetables, spinach, kale, rhubarb, almonds, cranberries, beets, and chocolates.[10]

3.2 Source of oxalate

There are two types of oxalate sources, exogenous and endogenous. Oxalate is an antinutrient present in a wide range of foods, with plant products, especially green leafy vegetables, being the main sources of dietary oxalates. Dietary oxalate is absorbed by the intestine from external sources. Between 20 and 40 percent of blood oxalate is dietary. Red blood cells, ascorbic acid, and liver are examples of endogenous sources. Metabolism produces oxalate.[11] Excessive produce of oxalate has the potential to induce high oxalate urine disease and encourage the development of oxalate stones. Hereditary glyoxylate metabolic abnormalities result in increased hepatic oxalate secretion, which causes primary hyperoxaluria (PH). Oxalate and oxalate precursors found in food be the factors that enhance the net absorption of oxalate in the gastrointestinal system (such as low calcium diet, poor fat absorption, and intestinal flora), are the causes of secondary hyperoxaluria.[12]

3.2.1 Exogenous sources of oxalate

Between 20 and 40 percent of the oxalate in plasma comes from food that the intestines absorb. Exogenous oxalate makes up a very small fraction of total plasma oxalate, yet it is extremely changeable and easily controlled by people due to its susceptibility to many variables. Preventing stone formation can be achieved by regulating exogenous oxalate. The majority of urinary oxalates were found to originate from the intestines, as evidenced by the significant improvement in hyperoxaluria that occurred after feeding the mice an oxalate-free diet.[13] Previous guideline suggests to limits oxalate intake to 40 to 50 mg each day with aim prevent kidney stone formation. The purpose of the low oxalate diet is to avoid super-saturation (excess concentration) of the urine with oxalate, therefore small amounts periodically are less harmful than large amounts.[14] Therefore, we need to comprehend how oxalate is absorbed in intestine and all factors influence this process.

3.2.2 Endogenous sources of oxalate

Oxalate generated by liver metabolism, or known as endogenous oxalate, accounts for 60–80% of plasma oxalate.[13] The body's oxalate precursor is broken down by the liver to create glyoxylate, which lactate dehydrogenase (LDH) subsequently transforms into oxalate. In the human body, alanine-glyoxylate aminotransferase (AGT) is a peroxisome enzyme that reduces endogenous oxalate synthesis by converting glyoxylate to glycine. 4-hydroxy-2-oxoglutarate aldolase (HOGA) is a crucial enzyme in the metabolism of hydroxyproline;[15] glyoxylate reductase–hydroxy-pyruvate reductase (GRHPR) likewise metabolizes glyoxylates and aids in limiting the synthesis of oxalates (Figure 1). Without these enzymes, the liver metabolizes glyoxylate to create an excess of endogenous oxalate, which raises the excretion of oxalate in the urine. Oxalate builds up in a number of organs. Primary hyperoxaluria is an uncommon autosomal recessive hereditary disorder affecting various organs, including the kidney [13]. Types 1, 2, and 3 of primary hyperoxaluria are caused by genetic deficiencies in AGT, GRHPR, and HOGA, respectively. The deposition of a significant amount of oxalate in the kidney due to primary hyperoxaluria causes kidney stones and deterioration of renal function, which in turn leads to end-stage renal disease.

Table 1. Human food containing high oxalate. [15]

Food	Oxalate (mg)/100 mg servings
Cereal or cereal products	
Wheat germ	269.0
Crackers, soybean	207.0
Grits (with corn)	41.0
Cake, fruit	11.8
Cake, sponge	7.4
Bread	4.9
Spaghetti with sauce	4.5
Cornflakes	2.0
Spaghetti boiled	1.5
Oatmeal, egg noodles	1
Milk or milk products	
Milk	0.15
Margarine, butter, cheese	0.0

Meats and eggs	
Liver	7.1
Fish sardines	4.8
Bacon, fried	3.3
Pork, roast	1.7
Ham	1.6
Vegetables	
Spinach, boiled	750.0
Beetroot, boiled	675.0
Swiss chard	45.0
Spinach, frozen	600.0
Pokeweed	476.0
Parsley	100.0
Leek	89.0
Collards	74.0
Sweet potatoes	56.0
Escarole	31.0
Celery	20.0
Squash	22.0
Fruits	
Chocolate	117.0
Lime peel	110.0
Green goose berries	88.0
Lime peel	83.0
Raspberries, black	53.0
Raspberries, red	15.0
Strawberries	15.0
Beverages	
Coca dry powder	623.0
Soybean	207.0
Tea	55.0-78.0
Coffee powder Nescafe	33.0
Ovaltine (2g/100ml)	10.0

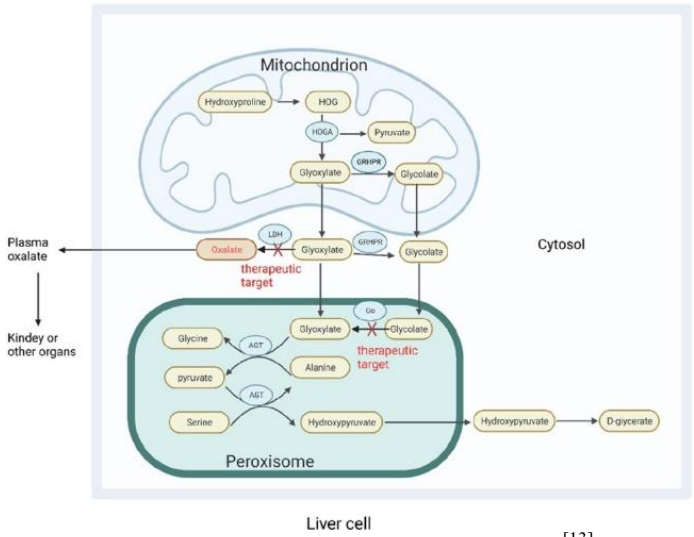

Figure 1. Metabolism oxalate in liver. [13]

3.3 Mechanism of oxalate absorption in the intestine

Research has demonstrated that oxalate can be passively absorbed in vitro at every stage of the digestive system. However, oxalate absorption is more likely in the stomach than in the small intestine or colon, although absorption at all sites is possible. This is due to changing conditions of pH and calcium concentration through

the gastrointestinal tract, depending on the form of oxalate in the food consumed and what other foods are consumed at the same time. Oxalate may be absorbed at that location if the food consumed contains oxalate in the soluble form and if the stomach's calcium concentration is low.[16] Based on the known solubility curve of CaOx versus pH at various concentrations of calcium, some food containing oxalate in the form of CaOx crystals would be predicted to dissolve at the normal gastric pH of F2. However, the amount that will dissolve is inversely proportional to the concentration of calcium. Therefore, the amount of calcium absorbed at the stomach site and the rate at which ingested CaOx dissolves will both decrease with increasing calcium concentration. While this is a minor factor in the stomach, magnesium may also be involved by complexing oxalate and reducing its availability for absorption.[17]

3.4 Oxalate excretion and kidney stone formation

Oxalate is a metabolic end product that needs to be eliminated from the body because it cannot be metabolized by the body's enzymes.[18] Renal and gastrointestinal excretion routes removed oxalate (Figure 2). SLC26A6, the most significant channel protein involved in oxalate transport, mediates oxalate production and absorption and is expressed in the kidney and intestine.[19][20] Renal calcium oxalate stones, hyperoxalemia, and hyperoxaluria are strongly associated with aberrant expression and function of SLC26A6 in the gut and kidney.[21] The kidney serves as the main excretory route for oxalate. Although renal tubular secretion can help with oxalate excretion glomerular filtration is the primary mechanism for oxalate excretion.[22]Urine oxalate concentration can rise due to increased oxalate production from renal tubular epithelial cells caused by SLC26A6 expression in the kidney. Due to oxidative stress, high oxalate concentrations in urine can harm renal tubular epithelial cells. These injured cells are more prone to crystal adhesion and aggregation. The development of oxalate stones is ultimately caused by a combination of two factors: renal tubule injury and oxalate oversaturation in urine.[23] One of the reasons for oxalate stones is elevated expression of SLC26A6 in the kidney; one possible preventative measure for oxalate stones is to downregulate SLC26A6. As a secondary route for the kidney's oxalate excretion, the intestinal tract plays a major role in controlling the total amount of oxalate absorbed by the digestive system, lowering the amount of oxalate excreted in the kidney, and avoiding the formation of oxalate stones. SLC26A6 is required to modulate oxalate secretion in the gut. Hyperoxalemia, hyperoxaluria, and oxalate stones were reported to be much more common in SLC26A6 KO mice by Zhirong Jiang *et al*. The mechanism could be that in mice with the SLC26A6 gene knockout, the intestine's net absorption of oxalate rises, the quantity of oxalate in the plasma. In healthy individuals, oxalate is readily filtered in the glomeruli and difficult to control; therefore, SLC26A6 is required to mediate the oxalate secretion of the renal tubules. As a result, variations in SLC26A6 expression can result in variations in oxalate secretion, and proximal tubule oxalate secretion may be impacted by SLC26A6 expression control. SLC26A6, which is found on the lumen side of the proximal tubule, uses Cl−/oxalate exchange, or oxalate secretion, to move oxalate from the cell to urine. Additionally, it can reabsorb oxalate by means of SO42−/oxalate exchange, which carries oxalate from urine into the cell.[17]

rises, and oxalate secretion is impaired because SLC26A6 is not able to operate properly.[24] Excretion of increased oxalate in the urine results in hyperoxaluria, which sets the stage for the development of oxalate stones. Oxalate excretions and homeostasis can describe in Figure 2.[25]

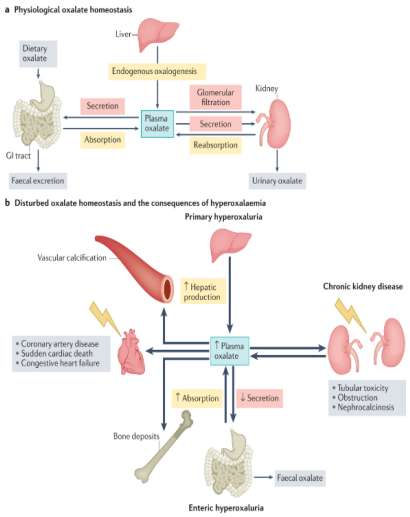

Figure 2. Homeostasis of oxalate.[31]

3.5 Low Oxalate Diet Affecting Kidney Stones Disease

Food frequency questionnaires and 24-hour urine collections have been two popular methods over the past few decades to investigate the role of dietary oxalate in stone risk. Regarding a patient's oxalate consumption and risk for stone disease, respectively, these two instruments provide insightful information. They do not, however, adequately evaluate the significant risk that could be connected to irregularly consuming high dietary oxalate intake. Three distinct long-term cohorts have had their potential stone formation examined using food frequency questionnaires. According to the research, there is a slight risk of stone disease [relative risk 1.21 for men and 1.22 for older women] while eating a diet high in oxalate.[13] Cooked and raw spinach was identified as the main source of dietary oxalate in these cohorts, despite rare usage. A typical amount of spinach (50–100 g) will result in a dietary oxalate load of around 500–1,000 mg and a marked increase in the excretion of oxalate in the urine.[14] The study may have understated the relationship between dietary oxalate and stone risk because of three factors: 1) participants' incapacity to precisely recall how frequently they ate foods high in oxalate over a one-month period; 2) variation in the quantity of oxalate-rich food consumed by a participant; and 3) variations in the absorption of the ingested oxalate.

3.6 Comparison of Researches

There are 10 studies that considered eligible for inclusion criteria in the Table 2.

Table 2. Comparison of Researches

Author	Method	Conclusion
Seeger *et al.,* 2017 [32]	Patients with CaOx stones were tested with low-sodium with low-calcium diet on the urinary risk profile	A diet low in sodium and calcium in recurrent calcium oxalate stone formers resulted in a significant reduction of urinary calcium excretion, but no change in urine volume.
Noori *et al.,* 2014 [33]	Patients with nephrolithiasis and hyperoxaluria was asked to follow a calorie-controlled Dietary Approaches to Stop Hypertension (DASH)-style diet whereas the control group was prescribed a low-oxalate diet	The DASH diet might be an effective alternative to the low-oxalate diet in reducing calcium oxalate supersaturation
Kaestner *et al.,* 2020 [34]	Patients with idiopathic hyperoxaluria were asked to adhere to a diet sheet which included general stone prevention advice and specific low oxalate diet advice.	General advice of low salt diet, increased water intake, moderate protein intake and specific oxalate restriction can significantly reduce oxalate excretion in hyperoxaluric stone formers.
Azimi *et al.,* 2020 [35]	Study that were interviewed about demographic and anthropometric information, medical history, physical activity, and dietary intake concluded into two dietary patterns (healthy and unhealthy)	Unhealthy dietary pattern was associated with the increased risk of calcium oxalate kidney stones, which is mostly due to the consumption of high calorie foods.
Kumar *et al.,* 2020 [36]	Healthy subjects consumed a controlled low-oxalate diet for 3 days before a dietary oxalate load. Urinary crystals were isolated by centrifugation and assessed using NTA before and 5 hours after the oxalate load. The morphology and chemical composition of crystals was assessed using electron microscopy, Fourier-transform infrared	NTA can quantify urinary nanocrystals and that meal rich in oxalate can promote nanocrystalluria. NTA should provide valuable insight about the role of nanocrystals in kidney stone formation.

	spectroscopy (FTIR), and ion chromatography-mass spectrometry (IC–MS).	
Langman *et al*., 2016 [37]	Subjects were healthy volunteers with hyperoxaluria that induced by high oxalate and low calcium (HOLC) ingestion and randomized to receive ALLN-177 as a treatment to reduce oxalate excretion compared with placebo.	Urinary oxalate excretion was greatly decreased by ALLN-177 therapy. This oral formulation demonstrates a novel management strategy for secondary hyperoxaluria.
Ariceta *et al*., 2023 [38]	Subjects were diagnosed primary hyperoxaluria with rare genetic diseases (eGFR <90 ml/min/1.73m^2) and randomized to receive Oxabact (oral formulation of lyophilized *O. formigenes* I) or Placebo to reduce plasma oxalate	Oxabact treatment showed a reduction in plasma oxalate when compared to placebo; however, after a year, the difference was not statistically significant. Kidney stones can be avoided by using *O. formingenes*, according to Oxabact therapy.
Quintero *et al*., 2020 [39]	Subjects were healthy volunteers who followed a 4-day high-oxalate diet plan (high oxalate intake: 750–800 mg/day) and low-calcium intake: 500–550 mg/day). They were randomized into two groups: those given 1000 U of Oxalate Decarboxylase (OxDC) and those given a placebo; the subjects' 24-hour oxalate excretion was calculated for each group.	Orally OxDC can effectively lower urine oxalate levels in healthy individuals following a high-oxalate diet without influencing creatinine clearance, urine creatinine, or other solutes associated with calcium oxalate supersaturation.
Masihi *et al.,* 2023 [40]	Subject were patients with recurrent calcium stone formation who had serum 25-hydroxyvitalim D level of 10-20 ng/mL. First group of participants received daily dose of 2000 IU oral cholecalciferol for 12 weeks compared to second group that received weekly dose of 50.000 IU oral cholecalciferol for 5 weeks and 24-hour urine calcium measurements to understand calcium phosphate or oxalate supersaturation were performed.	Both treatment regimens raised the amount of calcium in 24-hour urine, but they had no effect on the supersaturation condition of calcium phosphate or calcium oxalate.
Feraro *et al*., 2016 [41]	The study involved male and female healthcare professionals, both registered nurses, who were given dietary and supplementary ascorbic acid intake. The intervention was assessed in relation to an increased risk of kidney stones.	The risk of incident kidney stones was shown to be considerably greater in men who consumed both total and supplementary vitamin C, but not in women.

Research conducted by Seeger *et al.* shows that reducing sodium consumption in patients with CaOx stones in combination with a low calcium diet results in a significant reduction in urinary calcium excretion, but not a reduction in urine volume. Furthermore, calcium restriction in patients with low dietary calcium intake does not necessarily result in increased urinary oxalate excretion.[32] Noori *et al.* also stated that DASH diet could represent a novel strategy worthy of study in the prevention of high urinary calcium oxalate supersaturation, in addition to the conventional low-oxalate diet. Changes to the original DASH diet, including combining DASH with restricted oxalate intake, would be expected to boost the effectiveness of the original DASH diet for stone prevention.[33] In addition, low salt diet, increased water intake, moderate protein intake and specific oxalate restriction can significantly reduce oxalate excretion in hyperoxaluric stone formers.[34]

Based on research conducted by Azimi *et al*., many food groups and nutrients are associated with the risk of CaOx kidney stones, although evidences supporting the relationship between dietary patterns and CaOx kidney stone were limited. Unhealthy dietary pattern (high calorie, fat, and salt) increases the risk of CaOx kidney stone, although no association has been found between the healthy dietary pattern and the risk of CaOx kidney stone.[35] It has been suggested that consuming meals rich in oxalate can result in crystalluria. Increased urinary oxalate excretion can also increase stone risk by inducing renal tubule damage and disrupting protective urinary macromolecules.[36]

Previously mentioned, the development of oxalate kidney stonesis not only dependent on oxalate intake; other oxalate precursors, bacteria in the intestine, enzymes that aid in oxalate absorption. According to research by Langman *et al*., healthy patients with hyperoxaluria caused by high oxalate and low calcium (HOLC) diets that provide ALNN-177 have a considerable reduction in oxalate excretion. Individuals treated with ALLN-177 oral formulation had significantly lower oxalate excretion ($p=0.002$), with a mean reduction of 12.5 ± 16.5 mg/day. This Oral ALLN-177 is a recombinant oxalate decarboxylase enzyme obtained from *Bacillus subtilis* expressed in *Escherichia coli* reduce urinary oxalate excretion by degrading dietary oxalate in gastrointestinal tract and reducing its absorption.[37] Another study by Ariceta *et al.* demonstrates that supplementing with Oxabact can lower plasma oxalate in patients with rare genetic disorders associated with primary hyperoxaluria. Primary outcome did not significantly differ between groups that given placebo and Oxabact ($p=0.064$), even though participants treated with oxabact experienced a decrease in plasma oxalate levels, while those treated with a placebo experienced a constant or increased level. Although renal clearance is the main method of oxalate elimination, gastrointestinal tract excretion also occurs. Through promoting the secretion of oxalate from plasma into the intestine via the solute carrier anion transporter, SLC26, and facilitating the removal of endogenously produced oxalate from the blood, *Oxalobacter formingens* reduced plasma oxalate.[38] Based on Quentero *et al*., in addition to being linked to increased endogenous oxalate synthesis, decreased dietary calcium, hyperabsorption of oxalate, and excessive oxalate consumption in food, acid stabilized oxalate (OxDC) can also have an impact on hyperoxaluria controls. In healthy individuals after a high-oxalate diet, OxDC proves beneficial in lowering urinary oxalate levels.[39]

Vitamin D and Vitamin C both of which are oxalate precursors that influence oxalate absorption, can have an impact on oxalate levels. The prevalence of vitamin D deficiency (VDD) ranges from 18.9 to 59% among kidney stone formers who recur. Regarding the relationship between serum 25(OH)D and the condition of hypercalciuria, there were numerous discrepancies in earlier study. However, there has been worry that kidney stone patients receiving VDD treatment may benefit from cholecalciferol supplements. Supplementing with cholecalciferol can increase the quantity of calcium in 24 urines, but it has no effect on the supersaturation state of calcium phosphate or calcium oxalate, according to research by Masihi *et al*. [40] Based on research Ferarro *et al*., higher total and supplemental vitamin C intakes were not associated with an increased risk of incident kidney stones in the women's group, but they were in a significant portion of the men's group. Dietary vitamin C did not link with risk in any of the categories. We advise against giving vitamin C supplements to male calcium oxalate stone formers, but not dietary vitamin C [41]

4. Conclusion

Due to the high incidence and recurrence rate of kidney stones, many doctors now place more emphasis on treating them than on preventing them. Future research on kidney stone prevention should focus on etiology and pathology, as the importance of prevention cannot be emphasized. By addressing the source and excretion of oxalate specifically, kidney stones can be prevented from forming, one prevalent type being calcium oxalate stones. The likelihood of oxalate stones forming can also be decreased by eating a diet low in oxalate precursors and using an enzyme that lowers oxalate absorption.

References

[1] Alelign T, Petros B. Kidney Stone Disease: An update on current concepts. Advances in Urology. 2018:1–12. doi:10.1155/2018/3068365

[2] Sigurjonsdottir VK, Runolfsdottir HL, Indridason OS, Palsson R, Edvardsson VO. Impact of nephrolithiasis on kidney function. BMC Nephrology. 2015 Aug 28;16(1). doi:10.1186/s12882-015-0126-1

[3] Aggarwal KP, Narula S, Kakkar M, Tandon C. Nephrolithiasis: Molecular mechanism of renal stone formation and the critical role played by modulators. BioMed Research International. 2013:1–21. doi:10.1155/2013/292953

[4] Bhasin B. Primary and secondary hyperoxaluria: Understanding the Enigma. World Journal of Nephrology. 2015;4(2):235. doi:10.5527/wjn.v4.i2.235
[5] Taylor EN, Curhan GC. Determinants of 24-hour urinary oxalate excretion. Clinical Journal of the American Society of Nephrology. 2008 Sept;3(5):1453–60. doi:10.2215/cjn.01410308
[6] 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. 2016 May 26;45(2):177–83. doi:10.1007/s00240-016-0892-7
[7] Gnyawali D, Pradhan MM, Sigdel PR, Parajuli P, Chudal S, Poudyal S, et al. Efficacy of tamsulosin plus tadalafil versus Tamsulosin as medical expulsive therapy for lower ureteric stones: A randomized controlled trial. Advances in Urology. 2020 Jan 29;1–5. doi:10.1155/2020/4347598
[8] Finkielstein VA. Strategies for preventing calcium oxalate stones. Canadian Medical Association Journal. 2006 May 9;174(10):1407–9. doi:10.1503/cmaj.051517
[9] Heilberg IP, Schor N. Renal stone disease: Causes, evaluation and medical treatment. Arquivos Brasileiros de Endocrinologia & Metabologia. 2006 Aug;50(4):823–31. doi:10.1590/s0004-27302006000400027
[10] Alelign T, Petros B. Kidney Stone Disease: An update on current concepts. Advances in Urology. 2018;1–12. doi:10.1155/2018/3068365
[11] Marengo SR, Romani AM. Oxalate in renal stone disease: the terminal metabolite that just won't go away. Nat Clin Pract Nephrol. 2008 4:368–77. doi: 10.1038/ ncpneph0845
[12] Demoulin N, Aydin S, Gillion V, Morelle J, Jadoul M. Pathophysiology and management of hyperoxaluria and oxalate nephropathy: a review. Am J Kidney Dis. 2022; 79:717–27. doi: 10.1053/j.ajkd.2021.07.018
[13] Hoppe B. An update on primary hyperoxaluria. Nat Rev Nephrol. 2012; 8:467–75. doi: 10.1038/nrneph.2012.113
[14] Salido E, Pey AL, Rodriguez R, Lorenzo V. Primary hyperoxalurias: disorders of glyoxylate detoxification. Biochim Biophys Acta. 2012; 1822:1453–64. doi: 10.1016/j. bbadis.2012.03.004
[15] Salgado N, Silva MA, Figuera ME, Costa HS, Albuquerque TG. Oxalate in foods: extraction conditions, analitycal methods, occurrence, and health. Foods. 2023; 12:3201-21. doi.org/10.3390/foods12173201
[16] Jaeger PH, Rubertson WG. Role of dietary intake and intestinal absorbtion of oxalate in calcium stone formation. Nephron Physiology. 2004; 98:64-71. DOI: 10.1159/000080266
[17] Marengo, S. R., & Romani, A. M. Oxalate in renal stone disease: the terminal metabolite that just won’t go away. Nature Clinical Practice Nephrology. 2008;4(7):368–377.doi:10.1038/ncpneph0845
[18] Freel RW, Whittamore JM, Hatch M. Transcellular oxalate and Cl- absorption in mouse intestine is mediated by the Dra anion exchanger Slc26a3, and Dra deletion decreases urinary oxalate. Am J Physiol Gastrointest Liver Physiol. 2013; 305:G520–7. doi: 10.1152/ajpgi.00167.2013
[19] Knauf F, Ko N, Jiang Z, Robertson WG, Van Itallie CM, Anderson JM, et al. Net intestinal transport of oxalate reflects passive absorption and Slc26A6-mediated secretion. J Am Soc Nephrol. 2011; 22:2247–55. doi: 10.1681/ASN.2011040433
[20] Whittamore JM, Hatch M. The role of intestinal oxalate transport in hyperoxaluria and the formation of kidney stones in animals and man. Urolithiasis. 2017; 45:89–108. doi: 10.1007/s00240-016-0952-z
[21] Knauf F, Yang CL, Thomson RB, Mentone SA, Giebisch G, Aronson PS. Identification of a chloride-formate exchanger expressed on the brush border membrane of renal proximal tubule cells. Proc Natl Acad Sci U S A. 2001; 98:9425–30. doi: 10.1073/ pnas.141241098
[22] Crivelli JJ, Mitchell T, Knight J, Wood KD, Assimos DG, Holmes RP, Fargue S. Contribution of Dietary Oxalate and Oxalate Precursors to Urinary Oxalate Excretion. Nutrients. 2021; 13:62. https://doi.org/10.3390/nu13010062
[23] Lan Y, Zhu W, Duan X, Deng T, Li S, Liu Y, et al. Glycine suppresses kidney calcium oxalate crystal depositions via regulating urinary excretions of oxalate and citrate. J Cell Physiol. 2021; 236:6824–35. doi: 10.1002/jcp.30370
[24] Jiang Z, Asplin JR, Evan AP, Rajendran VM, Velazquez H, Nottoli TP, et al. Calcium oxalate urolithiasis in mice lacking anion transporter Slc26a6. Nat Genet. 2006; 38:474–8. doi: 10.1038/ng1762
[25] Ermer T, Nazzal L, Tio M.C. et al. Oxalate homeostasis. Nat Rev Nephrol. 2023; 19: 123–138. doi.org/10.1038/s41581-022-00643-3
[26] Khan SR, Canales BK, Dominguez-Gutierrez PR. Randall’s plaque and calcium oxalate Stone Formation: Role for immunity and inflammation. Nature Reviews Nephrology. 2021 Jan 29;17(6):417–33. doi:10.1038/s41581-020-00392-1
[27] Chen T, Qian B, Zou J, Luo P, Zou J, Li W, et al. Oxalate as a potent promoter of Kidney Stone Formation. Frontiers in Medicine. 2023 Jun 5;10. doi:10.3389/fmed.2023.1159616

[28] Taylor EN, Curhan GC. Oxalate intake and the risk for nephrolithiasis. Journal of the American Society of Nephrology. 2007 Jul;18(7):2198–204. doi:10.1681/asn.2007020219
[29] Holmes RP, Goodman HO, Assimos DG. Contribution of dietary oxalate to urinary oxalate excretion. Kidney International. 2001 Jan;59(1):270–6. doi:10.1046/j.1523-1755.2001.00488.x
[30] Curhan GC, Taylor EN. 24-H uric acid excretion and the risk of kidney stones. Kidney International. 2008 Feb;73(4):489–96. doi:10.1038/sj.ki.5002708
[31] Prochaska M, Taylor E, Ferraro PM, Curhan G. Relative supersaturation of 24-hour urine and likelihood of kidney stones. Journal of Urology. 2018 May;199(5):1262–6. doi:10.1016/j.juro.2017.10.046
[32] 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 Nephrology. 2017 Dec;18(1). doi:10.1186/s12882-017-0755-7
[33] Noori N, Honarkar E, Goldfarb DS, Kalantar-Zadeh K, Taheri M, Shakhssalim N, et al. Urinary lithogenic risk profile in recurrent stone formers with Hyperoxaluria: A randomized controlled trial comparing dash (dietary approaches to stop hypertension)-style and low-oxalate diets. American Journal of Kidney Diseases. 2014 Mar;63(3):456–63. doi:10.1053/j.ajkd.2013.11.022
[34] Kaestner L, Meki S, Moore A, van Woerden C, Lazarus J. General and dietary oxalate restriction advice reduces urinary oxalate in the stone clinic setting. S Afr J Surg. 2020;58(4):210-212.
[35] Kumar P, Patel M, Thomas V, Knight J, Holmes RP, Mitchell T. Dietary oxalate induces urinary nanocrystals in humans. Kidney International Reports. 2020 Jul;5(7):1040–51. doi:10.1016/j.ekir.2020.04.029
[36] Kumar P, Patel M, Thomas V, Knight J, Holmes RP, Mitchell T. Dietary oxalate induces urinary nanocrystals in humans. Kidney International Reports. 2020 Jul;5(7):1040–51. doi:10.1016/j.ekir.2020.04.029
[37] Langman CB, Grujic D, Pease RM, Easter L, Nezzer J, Margolin A, Brettman L. A Double Blind, Placebo Controlled, Randomized Phase 1 Cross-Over Study with ALLN-177, an orally administered oxalate degrading enzyme. American Journal of Nephrology. 2016 Aug;44(2): 150-158. doi.org/10.1159/000448766
[38] Ariceta G, Collard L, Schalk G. ePHex: a phase 3, double blind, placebo-controlled, randomized study to evaluate long term efficacy and safety of Oxalobacter formigenes in patients with primary hyperoxaluria. Pediatric Nephrology. 2023, 38:403-415. doi.org/10.1007/s00467-022-05591-5
[39] Quintero E, Yvonne V, Howard L, Gary S, Alan, R. A Prospective Double Blind, Randomized, Placebo Controlled, crossover study using an orally administered oxalate decarboxylase (OxDC). Kidney 360. 2020;1(11):1284-1290. doi.org/10.34067/KID.0001522020
[40] Masihi LS, Borumadnia N, Taheri M, Basiri A, Imani H, Jalali S, Tavasoli S. Effect of two vitamin D repletion protocols on 24-h urine calcium in patients with recurrent calcium kidney stones and vitamin D deficiency: a randomized clinical trial. European Journal of Medical Research. 2023;28(1): 246-255. doi.org/10.1186/s40001-023-01226-z
[41] Ferraro PM, Curhan GC, Gambaro G, Taylor EN. Total, dietary, and supplemental vitamin C intake and risk of incident kidney stones. American Journal of Kidney Diseases. 2016;67(3): 400–407. doi:10.1053/j.ajkd.2015.09.