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Nephrolithiasis – an updated review in relation to diagnosis, prevention and treatment

Abstract

Nephrolithiasis or urinary stone disease is a common problem across the world. Ample of research is going on in expedition for extenuating this disease condition. The procedure of preparing stones in the kidney, bladder or urethra is called as Nephrolithiasis. Stones form twice as often in men as women. The characteristic of stones that impede the renal pelvis is unbearable, blinking pain that goes from the flank to the groin or to the genital area and inner thigh. Control diet, use of prescribed medicines, and proper nutrient use can assist in thwart the development of kidney stones. Obe¬sity surge the threat of kidney stones. However, diminish in weight could deterrence of kidney stones if taken with a high ani¬mal protein intake. A vigilant medical and dietary history, stone analysis, serologic tests, and urine analysis comprise the preliminary screening in patients who have been identified with stones. Computed tomography and multi detector computed tomography played vital role in exploration of choice for the characterization of urinary stone disease. The appearance of dual–energy CT has further armoured the pre–eminence of this modality over other imaging techniques in the management of nephrolithiasis. This review is an effort to revitalize the previous data available for nephrolithiasis, basically work on its diagnosis and healing and endow with comprehensive and up–to–date information on area under discussion. This article also put light on synthetic drugs and medicines accessible for the mitigation of nephrolithiasis in the internationally and also discuss a part mentioning risk factors and management of nephrolithiasis.

Keywords: computed topography, cystine, hematuria, metabolic evaluation, medical exclusive therapy, pathophysiology

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Introduction

Nephrolithiasis is one of the main ailment of the urinary tract and is a chief source of morbidity. Stone formation is one of the painful urologic disorders that happen in approximately 15% of the global population and its re–occurrence rate in males is 74–86% and 45–62% in female. Kidney stones are linked with chronic kidney disease. Preventing reappearance is precisely to the type of stone like calcium oxalate, calcium phosphate, cystine, magnesium ammonium phosphate and uric acid stones.[1,2]

Renal stone formation and the biggest chemical stone composition depend on age and gender. The majority stones are formed in older age people. However, clinical interpretations have mentioned not only an altering frequency and composition of urinary calculi but also a swing in gender and age–related incidences. Contributing risk factors for kidney stones are obesity, insulin resistance and gastrointestinal pathology, living in warmer climates, and certain dietary patterns and medications.[3–6]

The escalating frequency of nephrolithiasis is associated with rising utilization of imaging for diagnosis, treatment planning, and post treatment follow–up. Imaging in nephrolithiasis has rise over the years due to technologic advancement and an improved understanding of the disease process. Since its beginning in the 1990s, unenhanced computed tomography has become the gold standard for the characterization of urinary stone disease.[7–9]

Classification of nephrolithiasis

Hypercalciuria

a. Absorptive hypercalciuria
b. Renal hypercalciuria
c. Resorptive hypercalciuria

Hyperuricosuric calcium nephrolithiasis

Hypocitraturic calcium nephrolithiasis

a. Chronic diarrheal syndrome
b. Distal RTA
c. Thiazide–induced

Hyperoxaluric calcium nephrolithiasis

a. Primary hyperoxaluria
b. Dietary hyperoxaluria
c. Enteric hyperoxaluria

Gouty diathesis

Cystinuria

Infection stones

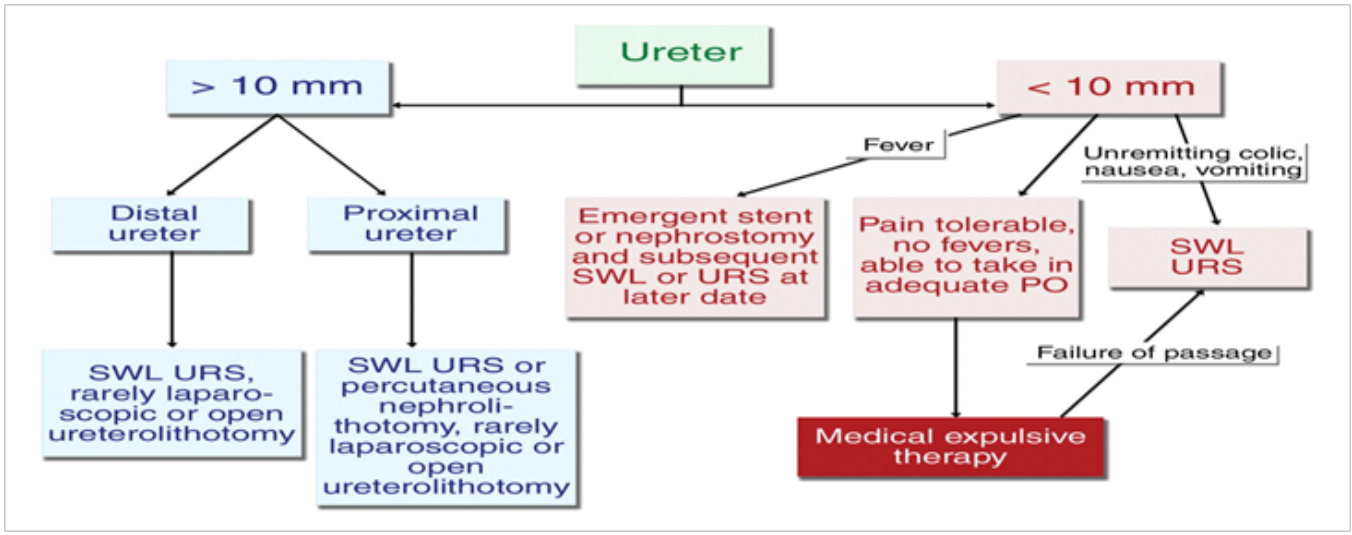

Figure 1 Therapeutic indication as per size (1 to 2cm) of kidney stones.

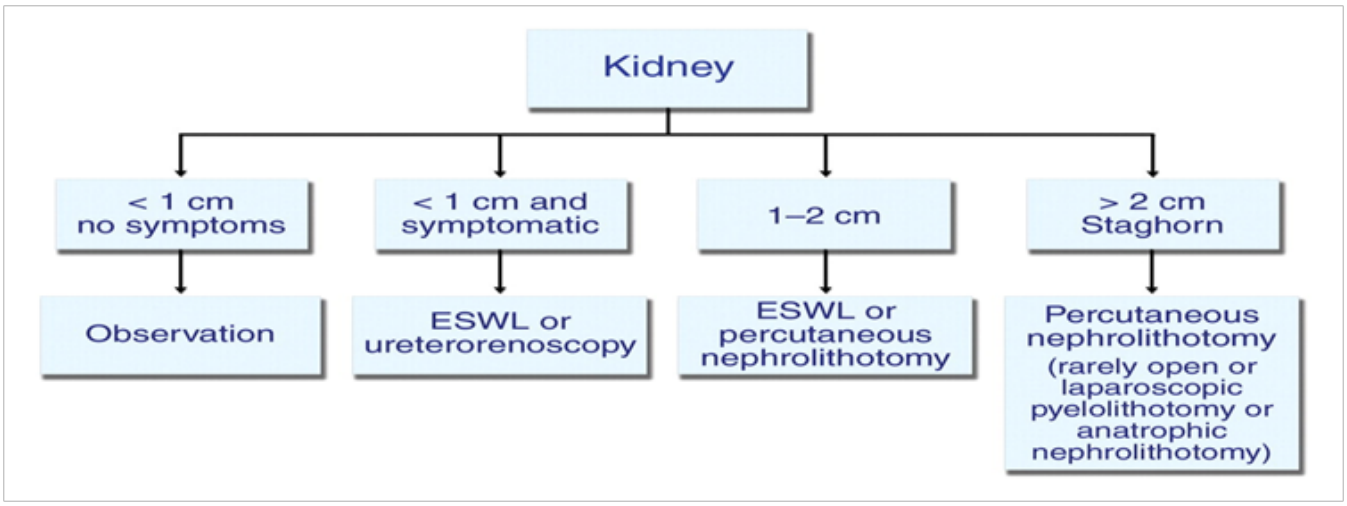

Figure 2 Therapeutic indication as per size (around 10cm) of kidney stones.

Kidney stone formation theories in the form of flow chart

Renal lymphatic system drains (renal pelvis)
↓
Prevents accretion and aggregation of precipitating salts (kidney)
↓
Mutilation or obliteration of renal lymphatics
↓
Salt precipitates
↓
Big concretions (passage through the lymph vessels)
↓
Concretions grind down the surrounding membrane eventually causing
↓
Urine percolation
↓
Invariable contact with the salts and other organic substances in the urine
↓
Develop into larger renal stones

Flowchart 1 Blocked lymphatic theory.[10,11]

Vasa recta and other capillaries (renal papillary region)
↓
Repeated bifurcations
↓
Quick changes from laminar to turbulent flow of blood
↓
Changes in hyperosmolar and hypoxic milieu
↓
Exposed to afflictions and injuries
↓
Result in the formation of atherosclerotic plaques in the vasculature of the renal papilla
↓
Calcification
↓
Erode their way into the renal interstitium and papillary ducts of Bellini
↓
Grow into larger stones on being in constant contact with the urine

Flowchart 2 Vascular theory.[12]

Stone formation as per anatomic site

There are quite a few diverse theories according to that stone formation happened in the kidney:

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i. Deposition of calcium on the basement membrane of collecting tubules and on the surface of papillae.

ii. Deposition of linear precipitates of calcium within the renal lymphatics to produce obstruction and breakdown of the membrane separating the lymphatics from the collecting tubules.

iii. Intratubular deposits of amorphous necrotic calcific cellular debris or organized mi–crocalculi (Table 1).

Crystals of one of the stone forming constituents

↓

Precipitate out of the supersaturated urine

↓

To aggregate or grow in size in the lumen of nephron

↓

Crystals retained at some distal or narrow portion of the nephron

↓

Act as a nidus for stone development.

Flowchart 3 Free particle theory.[13,14]

Crystals precipitate out of the supersaturated urine

↓

Attached to the renal epithelium at the site of renal tissue injury

↓

Caused due to infectious pathogens or crystals

↓

Attached to the renal epithelium

↓

Exposed to the supersaturated urine

↓

Act as foci for stone formation

Flowchart 4 Fixed particle theory.[15]

Stone formation takes place at the site of renal lesion.

↓

Form of renal lesions (due to apatite & increased urinary calcium levels)

↓

Constantly exposed to calyceal urine due to the loss of urothelium

↓

Apatite deposits termed as Randall's plaques

↓

Attract organic substances like lipids, glycosaminoglycans and urinary proteins form a matrix
Accumulate apatite crystals

↓

Coated with a layer of urinary proteins and other organic substances

↓

Forming a multilayered sandwich of apatite and organic matrix.

↓

Multiple layers then form an attachment site for calcium oxalate crystals

↓

Ultimately grow and form stones.

Flowchart 5 Randall's plaque hypothesis.[16–18]

Table 1 Proportion of percentage of kidney stones as per age factor

Type	Adults (%)	Children (%)
Uric Acid	10 to 16	1 to 3
Cystine	6 to 9	1
Calcium Phosphate	6 to 15	22 to 28
Magnesium Ammonium Phosphate	1 to 3	8 to 12
Calcium Oxalate	54 to 60	43 to 58

Stone formation theories

Crystallization and stone formation in urine engage a vastly complex process, the true nature of which is still scantily understood. The immense efforts devoted to the research of this condition have furnished so far only accessory information and do not seem to have penetrated the core of the problem.

Nucleation theory

Stone formation is initiated by the presence of a crystal or foreign body in urine supersaturated with a crystallizing salt that favours growth of a crystal lattice.

Randall's plaque theory

Randall in 1937 mentioned two kinds of calcific foci in the renal pyramids. Type I lesions were tiny calcified plaques located in the interstitial tissue below the surface epithelium of the renal papillae which progressively became exposed to the urine by the erosion of the epithelium overlying the plaque. Type II lesions contained of calcific masses found in the terminal parts of the ducts of Bellini.[19]

Vascular theory

Vasa recta and other capillaries in the renal papillary region, due to their repeated bifurcations are prone to quick changes from laminar to turbulent flow of blood, which is similar to as seen with the bifurcated arteries. Owing to this repeated blood flow changes as well as their hyperosmolar and hypoxic milieu, they are exposed to afflictions and injuries and as is case with arteries, these blood flow changes and vulnerable tissue structures result in the formation of atherosclerotic plaques in the vasculature of the renal papilla followed by calcification.[11]

Blocked lymphatic theory

The theory describes that renal lymphatic system drains the renal pelvis and prevents accretion and aggregation of precipitating salts in the kidney. But in case of destruction of these renal lymphatics, salt precipitates tend to grow into big concretions during their passage through the lymph vessels and get thwarted at the fornices of the calyces just outside the collecting system where the concretions eventually grind down the surrounding membrane ultimately causing urine percolation and then grow into big renal stones by being in constant contact with the salts and other organic substances in the urine.[12]

Diagnostic characterization

Symptoms & signs at presentation

Symptoms related to stones at specific sites:

i. Caliceal stones

ii. Renal pelvic stones

iii. Proximal ureteral stones

iv. Distal uretheral stones

Associated non renal symptoms

Variability of symptoms

Finding on physical examination

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Radiographic findings

i. Intravenous urography

ii. Tomography

iii. Retrograde urography

iv. Ultrasonography

v. CT scanning

Surgical treatment for renal stones:

a. Hypothermia in urologic surgery

b. Intraoperative X rays

Open surgical procedures:

a. Nephrectomy and partial nephrectomy

b. Pyelolithotomy

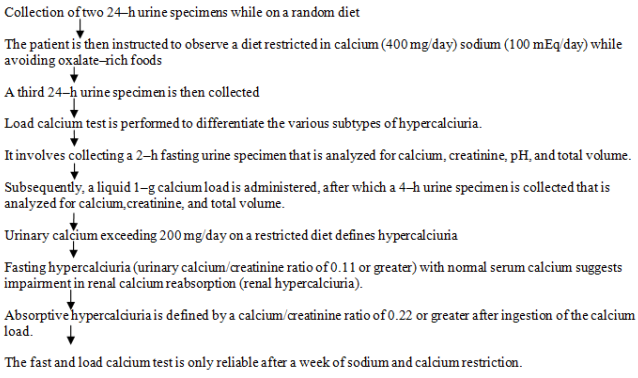
c. Extended Pyelolithotomy

d. Pyelonephrolithotomy

e. Coagulum Pyelolithotomy

f. Anatropic Nephrolithotomy

g. Radial nephrotomy



Flowchart 6 Metabolic evaluation.[20,21]

Role of individual weight on kidney stone

Obesity plays a vital role in kidney stones more than dietary factors. The related changes in body composition pretence biophysical challenges linked with troubled thermogenesis and dehydration. The part of body water diminishes due to hydrophobicity of body fat with escalating obesity, by which dehydration surge. Addition to that, the dwindle in surface area to body volume make difficult heat exchange and metabolic rate. Obesity is a proinflammatory state related to electrolyte imbalances and transformed urine chemistry. Fatty persons with kidney stones are exposed to hyperuricemia, gout, hypocitraturia, hyperuricosuria, and uric acid stones. A current retrospective investigation found that patients with diabetes and kidney stones emit more oxalate and have lower urine pH, which is partially an outcome of elevated sulfate excretion and fewer acid emitted as ammonium ions.[22–24]

Role of fructose intake

Escalated fructose intake surges urinary calcium excretion in persons with magnesium deficiency, and fructose is the barely dietary carbohydrate known to raise uric acid levels. Augmented dietary fructose has been related with up to a 40 percent high risk of kidney stones. However, sugar–sweetened beverages and orange juice also play important role to gout.[25,26]

Kidney stone and alkaline urine

Eating a diet high in fruits and vegetables produces alkalinizing urine. For impediment of calcium oxalate, cystine, and uric acid stones, urine should be alkalinized. Western diets are characteristically high in acid–producing foods, such as grains, dairy products, legumes, and meat. So more problems associated with kidney stones in those countries.[27,28]

Low urine pH and kidney stone

Sodium chloride sinks urine pH but it can snowball the blood pressure, insulin excretion, and urine calcium excretion. For deterrence of calcium phosphate and struvite stones, urine should be acidified. Cranberry juice or betaine can dwindle the urine pH without the undesirable effects related to with foods with acidic environment.[29]

Treatment of nephrolithiasis

a) Non–steroidal anti–inflammatory drugs (NSAIDs) and opioids are used to relieve pain associated with nephrolithiasis.[30]

b) Medical expulsive therapy is used to allow spontaneous expulsion of moderately sized distal ureteral calculi from the urinary tract. Offer α–blockers as MET as one of the treatment options, in particular for (distal) ureteral stones>5mm.[31]

c) Allopurinol is prescribed for the treatment of calcium oxalate and uric acid stones.[32]

d) Thiazide and related diuretics are indicated in renal stone disease associated with idiopathic hypercalciuria.[33]

e) Acetohydroxamic acid is prescribed in case of struvite stones that are usually formed due to or are associated with the UTI caused by urease producing organisms.[34]

f) D–penicillamine is used in case of cystine stones for treating cystinuria.[35]

g) Alpha mercaptopropionylglycine (or tiopronin) is a better tolerated alternative to D–penicillamine, but its efficacy and availability is very less as compared to D–penicillamine.[36]

h) Potassium citrate basically raises urinary citrate levels. Citrate complexes urinary calcium to a soluble form, thus inhibiting calcium phosphate and calcium oxalate crystal aggregation.[37]

i) Chemolytic dissolution therapy is a dissolution technique that aims at the dissolution and removal of urinary stones via pH alteration, chelation and disulphide rearrangement.[38]

j) Sodium cellulose phosphate is known to bind to intestinal calcium and thus inhibit absorption of calcium leading to reduction in the elevated calcium excretion thus reducing calcium stone formation.[39]

k) Acetohydroxamic acid is prescribed in case of struvite stones that are usually formed due to or are associated with the UTI caused by urease producing organisms.[40]

l) Chemolytic dissolution therapy can be used as an adjunct

to extracorporeal shock wave lithotripsy and Percutaneous nephrolithotomy, or can also be used to completely avoid surgery (Table 2–4).[41]

Table 2 Medicines used to plummet kidney stone formation

Type of formulations/medicines	Examples
Potassium Sparing Diuretics	Triamterene
Antibiotics	Sulfonamides, Amoxicillin, Ceftriaxone
Carbonic Anhydrase Inhibitors	Acetazolamide, Topiramate
Uric Acid Production Decrement	Allopurinol
Sulfonyl Ureas	For type 2 diabetes mellitus
Potassium Channel Blockers	Amiodarone, Sotalol

Table 3 Management of kidney stones in adults

Management Type	Suggestive approach or therapies
Pain management	Codeine, Acetaminophen, Hydrocone
Fluids	Oral intake of water, Intravenous saline if patient is unconscious
Antispasmodics	Doxazosin, Tamsulosin, Nifedipine,

Table 4 Treatment of various clinical indications of nephrolithiasis

Clinical indications	Treatment
Common	
Stone less than 1cm in kidney	Shock wave lithotripsy
Stone less than 1cm in kidney in women	Ureteroscopy with lithotripsy (semi rigid)
Stone less than 1cm in proximal ureter, stones less than 1.5 cm in kidney	Ureteroscopy with lithotripsy (flexible)
stones greater than 1.5cm in kidney or proximal ureter	Percutaneous nephrolithotomy
Uncommon	
Large stone in middle or distal ureter	Open or laparoscopic ureterolithotomy
Larges tones in horseshoe kidney	Open or laparoscopic ureterolithotomy
Full staghorn calculi	Anatrophic nephrolithotomy

Conclusion

Nephrolithiasis is a frequent disease with an escalating occurrence and pervasiveness worldwide. Lifestyle and dietary choices concerned in the complex of the metabolic syndrome are imperative factors contributing to such developments. Keeping a close watch on one's body weight, maintaining healthy routine and healthy diet that includes vegetables, fruits, fibres and adequate amount of fluids is forever a good call not only when it comes to preventing nephrolithiasis but any ailment condition, because these are the indices that when compromised might lead to one or the other health impairments. Metabolic evaluation is a significant component of management for patients with nephrolithiasis. Although empiric drug therapy may give effectual prophylaxis against stone recurrence, treatment based on metabolic evaluation allows classification of patients into simple diagnostic groups to which an uncomplicated treatment algorithm can be applied in a cost–effective manner. In addition, characterization is beneficial because of the supplementary medical information it gives. Multidetector CT currently plays an imperative management role in patients with urolithiasis, from the initial diagnosis in patients with acute flank pain to treatment planning and posttreatment follow–up.

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Conflict of interest

The author declares no conflict of interest.

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