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. Obesity surge the threat of kidney stones. However, diminish in weight could deterrence of kidney stones if taken with a high animal 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 imaging 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

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
- Absorptive hypercalciuria
- Renal hypercalciuria
- 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

Figures 1 & 2

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

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

Kidney Stone Formation Theories in the Form of Flow Chart

Flowcharts 1-5

Stone Formation as Per Anatomic Site

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

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 microcalculi (Table 1).

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

<table>
<thead>
<tr>
<th>Type</th>
<th>Adults (%)</th>
<th>Children (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric Acid</td>
<td>10 to 16</td>
<td>1 to 3</td>
</tr>
<tr>
<td>Cystine</td>
<td>6 to 9</td>
<td>1</td>
</tr>
<tr>
<td>Calcium Phosphate</td>
<td>6 to 15</td>
<td>22 to 28</td>
</tr>
<tr>
<td>Magnesium Ammonium Phosphate</td>
<td>1 to 3</td>
<td>8 to 12</td>
</tr>
<tr>
<td>Calcium Oxalate</td>
<td>54 to 60</td>
<td>43 to 58</td>
</tr>
</tbody>
</table>

Stone Formation Theories

Crystallization and stone formation in urine engage a vastly complex process, the true nature of which is still scantly 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.
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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.

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 fornice 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 ureteral stones

**Associated non renal symptoms**

**Variability of symptoms**

**Finding on physical examination**

**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

g. **Radial nephrotomy**

Flowchart 6

**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 present 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 that aims at the dissolution and removal of urinary stones via pH alteration, chelation and disulphide rearrangement [37].

**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 > 5 mm [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 [41] (Table 2-4).

### Table 2: Medicines used to plummet kidney stone formation.

<table>
<thead>
<tr>
<th>Type of Formulations/Medicines</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium Sparing Diuretics</td>
<td>Triamterene</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Sulfonamides, Amoxicillin, Ceftriaxone</td>
</tr>
<tr>
<td>Carbonic Anhydrase Inhibitors</td>
<td>Acetazolamide, Topiramate</td>
</tr>
<tr>
<td>Uric Acid Production Decrement</td>
<td>Allopurinol</td>
</tr>
<tr>
<td>Sulfonyl Ureas</td>
<td>For type 2 diabetes mellitus</td>
</tr>
<tr>
<td>Potassium Channel Blockers</td>
<td>Amiodarone, Sotalol</td>
</tr>
</tbody>
</table>

### Table 3: Management of kidney stones in adults.

<table>
<thead>
<tr>
<th>Management Type</th>
<th>Suggestive Approach or Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain management</td>
<td>Codeine, Acetaminophen, Hydrocone</td>
</tr>
<tr>
<td>Fluids</td>
<td>Oral intake of water, Intravenous saline if patient is unconscious</td>
</tr>
<tr>
<td>Antispasmodics</td>
<td>Doxazosin, Tamsulosin, Nifedipine.</td>
</tr>
</tbody>
</table>

### Table 4: Treatment of Various clinical indications of Nephrolithiasis.

<table>
<thead>
<tr>
<th>Clinical Indications</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stone less than 1 cm in kidney</td>
<td>Shock wave lithotripsy</td>
</tr>
<tr>
<td>Stone less than 1 cm in kidney in women</td>
<td>Ureteroscopy with lithotripsy (semi rigid)</td>
</tr>
<tr>
<td>Stone less than 1.5 cm in kidney</td>
<td>Ureteroscopy with lithotripsy (flexible)</td>
</tr>
<tr>
<td>Stones greater than 1.5 cm in kidney or proximal ureter</td>
<td>Percutaneous nephrolithotomy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Indications</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large stone in middle or distal ureter</td>
<td>Open or laparoscopic ureterolithotomy</td>
</tr>
<tr>
<td>Larges tones in horseshoe kidney</td>
<td>Open or laparoscopic ureterolithotomy</td>
</tr>
<tr>
<td>Full staghorn calculi</td>
<td>Anotrophic nephrolithotomy</td>
</tr>
</tbody>
</table>

### Conclusion

**Nephrolithiasis** is a frequent disease with an escalating occurrence and perversiveness 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 authors declare no conflict of interest.

References

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