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KIDNEY STONES: FROM PATHOGENESIS TO PREVENTION - A CRITICAL REVIEW

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Abstract:

The goal of this review was to assemble the most recent data on kidney stone etiology, pathophysiology, and preventative strategies. One of the earliest recognized medical disorders in human history is kidney stone illness, sometimes referred to as nephrolithiasis or urolithiasis. It is a growing urological condition that affects roughly 12% of people worldwide. An imbalance between factors that either promote or inhibit urinary crystallization modulates the multifactorial mechanism of kidney stone formation, a complex process that arises from multiple physicochemical events such as supersaturation, nucleation, growth, aggregation, and retention of urinary stone steps. A higher incidence of urolithiasis is associated with lifestyle variables like sedentary behavior, a high body mass index, and bad eating habits, as well as medical disorders like diabetes and dyslipidemia. In order to diagnose kidney stones, guide treatment choices, and maybe lessen the need for surgery, radiological imaging is essential. This reduces hospital stays and related consequences. By combining data from peer-reviewed literature, this review thoroughly assesses the effectiveness of several radiological imaging modalities in identifying and treating urolithiasis in a range of clinical settings.

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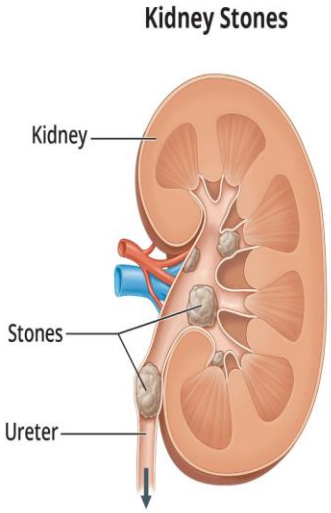
INTRODUCTION:

Kidney stones (calculi) are mineral deposits that form in the renal calyces and pelvis and can be found either freely or attached to the renal papillae. In contrast, diffuse calcification of the renal parenchyma is referred to as nephrocalcinosis. Stones that form in the urinary tract (also known as nephrolithiasis or urolithiasis) develop when urine becomes overly saturated with minerals, leading to crystal formation, growth, aggregation, and retention within the kidneys.



Globally, about 80% of kidney stones are composed of calcium oxalate (CaOx) mixed with calcium phosphate (CaP). Kidney stone disease, also called nephrolithiasis or urolithiasis, is a condition in which soluble substances in the urine form solid, crystalline materials in the urinary tract, leading to formation of stones. The occurrence of this condition has been rising, along with changes in who is affected. Previously seen as a problem with periodic flare-ups that could be handled by urologists, nephrolithiasis is now understood as a more complex issue that needs detailed assessment and comprehensive treatment. Stones made of uric acid, struvite, and cystine are also commonly found, accounting for roughly 9%, 10%, and 1% of stones, respectively.

There has been significant progress in the medical and surgical treatment of kidney stone patients. Stones can be broken up using shockwave lithotripsy (SWL) to help them pass through urine, or surgically removed via percutaneous nephrolithotomy (PCNL) or retrograde intrarenal surgery (RIRS).

EPIDEMIOLOGY:

Around the world, the number of people getting kidney stones and the chances of them happening again are going up, and there aren't many strong medicines available to treat them. About 12% of people worldwide will get kidney stones at some point in their lives. It can affect anyone, regardless of age, gender, or race, but it happens more often in men than in women between the ages of 20 and 49. If people don't take preventive measures, the chance of getting another stone within a year is about 10 to 23%, and it goes up to 50% in 5 to 10 years, and 75% after 20 years. Even though the overall risk of kidney stones is higher in men, more women are now developing stones. Because of this, taking steps to prevent stones is very important for managing the condition.

Recent research shows that the number of people getting urinary stones has been going up over the last few decades in both rich and poor countries. This increase is thought to be linked to lifestyle factors like not exercising enough and changes in what people eat, as well as rising temperatures around the world. In the U.S., about 1 out of every 11 people has kidney stone, and around 600,000 people in the country deal with urinary stones each year. In India, about 12% of the population is expected to develop urinary stones, and of those, roughly half may end up losing kidney function.

ETIOLOGY & RISK FACTORS:

Kidney stones form because of many different reasons that involve both things you are born with and things in your environment. Some of these include your age, gender, and family history. Other factors are related to where you live, the weather, what you eat, the minerals in your food, and how much water you drink.

METABOLIC FACTOR:

Crystals that aggregate into stones can occur as a result of imbalances in the composition of urine. Significant contributions are made by elements such hyperoxaluria (high oxalate levels), hyperuricosuria (high uric acid levels), hypocitraturia (low citrate levels), and hypercalciuria (high calcium levels in urine).

GENETIC FACTOR:

Kidney stones are more likely to form in people with certain genetic abnormalities, such as cystinuria and hyperoxaluria. These disorders alter how chemicals like cystine and oxalate are metabolized, increasing the risk that stones will form from their excretion.

ENVIRONMENTAL FACTORS:

A number of environmental factors influence the formation of stones, including geographic location (areas with high incidence rates due to water composition), occupation (involving exposure to specific chemicals), and climate (hot and dry climates can cause dehydration and concentrated urine).

DIETARY FACTOR:

Consuming a lot of foods high in purines (which raise the production of uric acid), oxalate (such as

spinach and almonds), and sodium can cause stones to develop. Urine volume is decreased by inadequate fluid consumption, which raises the concentration of chemicals that cause stones.

ANATOMICAL FACTOR:
Kidney malformations or narrow ureters are examples of structural abnormalities in the urinary tract that can impede urine flow and encourage the production of stones.

MEDICAL DISEASE:
A number of medical diseases raise the incidence of kidney stones, including metabolic disorders including hyperparathyroidism, inflammatory bowel disease, and recurrent UTIs.

METABOLIC RISK FACTORS:
Hypercalciuria (40-60%)
Hyperuricosuria (25%)
Hyperoxaluria
Hypocitriuria
Other (hot climates, urinary tract anomalies)

HYPERCALCIUREA:
Hypercalciuria is characterized by urinary calcium excretion exceeding 200 mg in a 24-hour collection or an excess of 1 mmol calcium/kg/24 h. It is the most common metabolic abnormality in patients with calcium-containing stones and results from various mechanisms.

HYPERURICOSURIA:
Uric acid is the end result of breaking down purines, which come from both the food we eat and from the body's own cells as they break down.
Stones made entirely of uric acid are not very common but tend to come back again and again. A low level of acid in the urine, is the most common and important reason for forming uric acid stones in the kidneys. If someone has had gout in the past, their chance of developing kidney stones is twice as high.

HYPEROXALURIA:
Hyperoxaluria is defined as urinary excretion of oxalate exceeding 45 mg/day.

HYPOCITRIURIA:
Urinary citrate excretion of less than 250 mg in a 24-hour period is known as hypocitriuria. Together with calcium, urinary citrate produces a soluble compound that prevents crystal formation and growth. Compared to men, women have a lower incidence of stone formation and excrete more citrate. The primary exogenous sources of urine citrate are fruits like grapefruits and oranges.

CLINICAL MANIFESTATIONS:
Signs and symptoms associated with urolithiasis diseases depending on whether the kidney stone is inside the bladder, ureter, or kidney, the symptoms vary. There are initially no symptoms associated with stone formation.
Consequently, indications and symptoms of stone disease include -

- Colicky pain is one indication of kidney stones
- Hydronephrosis (dilation of the kidney)
- Flank pain (back discomfort)
- Urinary tract infections
- Renal colic (severe cramping pain)
- Haematuria (bloody urine)
- Nausea, and vomiting
- Pyuria
- Dysuria
- Oliguria

MECHANISM OF RENAL STONE FORMATION:
Biomineralization, another name for kidney stone pathogenesis, is a complex biochemical process that is still not fully understood. Urine supersaturation and physicochemical changes are two biological processes involved in the development of kidney stones. If there is more dissolved material in a solution than the solvent could typically dissolve, the solution is said to be supersaturated. Urine that is supersaturated experiences solute precipitation, which sets off nucleation and the development of crystal concretions. Stated differently, crystallization occurs when the concentration of two ions in a solution exceeds their saturation point.

PROMOTORS OF STONE FORMATION:
Ions such as calcium, phosphate, urate, and oxalate encourage crystallization and aggregation.

INHIBITORS OF STONE FORMATION:
These inhibitors consist of metallic cations (like magnesium), anions (like citrate), and alkali supplements.

- **Nucleation**
  When solid crystals begin to form in a solution due to nucleation, kidney stones begin to form. A solution is said to be supersaturated if it contains more dissolved material than normal solvency permits. The energy required for crystallization can be reduced by either heterogeneously produced by promoters on pre-existing surfaces or homogeneously occurring inside unstable supersaturation zones, which is essential in renal stone genesis. As additional constituents combine to form the crystal structure, the free energy of the solution

decreases as the crystal grows. Crystalline particles can form bigger structures by binding in random or directed ways.

- **Crystal growth**
  After nucleation, microcrystals grow epitaxially, in which one crystalline substance aligns and expands on the lattice of another substrate.
  This method involves both heteroepitaxial development, in which crystals form directly on surfaces with varying compositions, and monoepitaxial growth, in which molecules or ions from supersaturated urine adsorb successively onto a crystal surface.
  Atoms or molecules start to group together in a supersaturated liquid, and surface energy raises the total free energy, particularly in smaller clusters. Size, shape, material characteristics, pH, and structural flaws are all important aspects of particle formation that affect crystal growth.
- **Aggregation**
  Crystal nuclei link together to form bigger particles during aggregation, which is facilitated by additional salt addition. Particle aggregation is favored when interparticle distances are close because they increase attractive forces. In stone formation, when aggregation frequently dominates nucleation and growth stages, this mechanism is crucial. In addition to inter-particle distances that encourage aggregation, factors that balance aggregation and disaggregation effects also affect aggregation dynamics in solution.
- **Retention**
  The attachment of crystals to the lining epithelial cells may result in crystal retention. Crystal production, retention, and accumulation in the kidney are necessary for urolithiasis. Crystal retention is another process that could result in the production of stones. i.e., crystal development, precipitation, and aggregation, which leads to the formation of urinary stones, if the nucleated crystals were removed by urine flow , stones don't form.

TYPES OF KIDNEY STONES:

The makeup of kidney stones is linked to the unusual levels of different chemicals in urine. Each type of stone can vary in how big it is, its shape, and what chemicals it contains. Because of the different types of minerals and how they form, kidney stones are usually grouped into five main types. These are:

- Calcium Stones
- Struvite or Magnesium Ammonium Phosphate Stones
- Uric Acid Stones or Urate Stones
- Cystine Stones
- Drug-Induced Stones

- **CALCIUM STONES:**
  Calcium stones are the most common type of kidney stones, making up about 80% of all urinary stones. These stones are mainly made up of two types: calcium oxalate and calcium phosphate. About 50% of calcium stones are pure calcium oxalate, 5% are pure calcium phosphate, and 45% are a mix of both. Calcium oxalate is the most common form found in kidney stones. It can be in the form of calcium oxalate monohydrate (COM) or calcium oxalate dihydrate (COD), or both together. COM is more commonly found in stones than COD.
- **STRUVITE STONES:**
  Struvite or magnesium ammonium phosphate stones make up 10 to 15 percent of all stones. These are also called infection stones or triple phosphate stones. They form in people who have long-term urinary tract infections caused by bacteria that produce urease. The most common bacteria is Proteus mirabilis, but others like Klebsiella pneumonia, Pseudomonas aeruginosa, and Enterobacter can also cause them. Urease helps break down urea into ammonia and carbon dioxide, making the urine more alkaline and increasing its pH, which is typically above 7.
- **URIC ACID STONES:**
  Uric acid stones, also called urate stones, make up about 3 to 10% of all types of kidney stones. Eating a lot of purines, especially from animal proteins like meat and fish, can lead to high levels of uric acid in the urine, less urine output, and a lower urine pH (pH below 5.05), which makes it easier for uric acid stones to form. People with gout arthritis may also develop stones in their kidneys. The most common reason for uric acid stones is unknown, called idiopathic, and these stones are more common in men than in women.
- **CYSTINE STONES:**
  Cystine stones make up less than 2% of all kidney stones. They are linked to a genetic problem that affects how the body handles an amino acid called cystine. This condition, known as cystinuria, causes too much cystine to be passed in urine. Cystinuria is an inherited disorder that follows an autosomal recessive pattern. It

happens because of a problem with the rBAT gene located on chromosome 2. This gene defect stops the kidneys from properly absorbing cystine, allowing it to leak into the urine.

- **DRUG- INDUCED STONES:**
  Drug-induced stones make up around 1% of all kidney stones. Certain medications, like guaifenesin, triamterene, atazanavir, and sulfa drugs, can cause these stones. For example, people taking indinavir sulfate, which is used to treat HIV, are more likely to get kidney stones. These drugs or their breakdown products can stick to the kidneys and start forming stones, or they can attach to existing stones. Also, these medicines might lead to stone formation by changing how the body handles calcium oxalate or purines.

DIAGNOSTIC TECHNIQUES:

- Computed tomography
- Urinalysis
- Ultrasonography
- Magnetic resonance urography

PREVENTION:

Options for Preventing Urolithiasis Resolving the root cause of kidney stones is essential to their prevention. Usually, medication and appropriate nutrition control are needed to avoid kidney stone formation's initial or subsequent episodes. The most effective way to avoid urolithiasis is to regulate nutrition and prevent kidney stone disease by dietary intervention.

- Hydration
- Low-oxalate diet
- Maintain calcium intake
- Limiting consumption of animal proteins
- Stay away from foods high in vitamin D
- Increase consumption of potassium-rich fruits and vegetables.
- Minimize vitamin C intake

STONE SPECIFIC PREVENTION:

1. **calcium oxalate, cystine, and uric acid stones.**
   Consuming a diet rich in fruits and vegetables, taking prescription or supplemental citrate, or drinking alkaline mineral waters can all help to alkalinize urine.
2. **cystine stone**
   Protein and sodium consumption must be limited
3. **uric acid stone**
   gout must be managed for uric acid stone formers.
4. **calcium phosphate and struvite stones.**
   Urine should be acidified. Patients need to be closely monitored to ensure that the infection has subsided.

MANAGEMENT:

Surgical management:

SHOCKWAVE LITHOTRIPSY:

High-energy acoustic waves are delivered non-invasively during SWL in order to break up a kidney stone. An acoustic lens is used to focus the shockwave, which is produced by electrohydraulic, electromagnetic, or other energy sources, on the stone after passing through the patient. During SWL, fluoroscopic or ultrasonographic guidance is frequently utilized to help in precise targeting and for accurate acoustic-wave focusing. General anesthesia or deep sedation are frequently utilized to regulate respiratory and renal activity and provide intraoperative analgesia.

URETEROSCOPIC FRAGMENTATION AND RETRIEVAL:

In order to access the stone and administer additional tools like guidewires, balloon dilators, laser fibers, and baskets, ureteroscopy involves retrogradely passing an endoscope from the urethra proximally towards the damaged ureter and kidney. Despite being relatively non-invasive, spinal or general anesthesia is necessary for ureteroscopy in order to reduce pain and the visceral reaction to renal and ureteral dilatation. Compared to SWL, ureteroscopic retrieval had a greater rate of kidney and ureteral stone-free outcomes and a reduced requirement for retreatment, according to a recent meta-analysis. SWL and ureteroscopy are therefore regarded as first-line treatments for ureteral stones smaller than 10 mm. Ureteteroscopic fragmentation produces greater stone-free rates and fewer procedures for ureteral stones larger than 10 mm.

PERCUTANEOUS NEPHROLITHITOMY:

PCNL, which is often used for stones larger than 2 cm, entails the direct percutaneous passage of an endoscope via the skin, muscle, and perirenal fat into the kidney. The kidney is found using anatomical marks when the patient is in either the prone or supine position while under general anesthesia. Under the direction of fluoroscopic and/or ultrasonographic procedures, renal access can be accomplished in conjunction with endoscopic or radiographic imaging methods. a posterior calyx puncture using a needle. In the 80–90% range, PCNL often gives extremely high stone-free rates. Although PCNL is more intrusive, it is thought to be more effective than SWL or ureteroscopic treatments for the majority of stones.

CONCLUSION:

Finally, this thorough review work has given a summary of new ideas about the mechanisms behind the formation of stones. The most recent studies on metabolic risk factors, kidney stone disease-related receptors, promoters, and inhibitors were included. Renal stone development has several unanswered questions. Crystal retention, cell apoptosis, renal cell damage, and related stone inhibitors or promoters all undoubtedly contribute to the development of kidney stones. Furthermore, urolithiasis mechanisms linked to stone inhibitors or promoters must be better understood in order to develop medications that remove stones. Additionally, knowing the pathophysiology, etiology, and genetic basis of kidney stone development can help researchers find new medications and treatment approaches for urolithiasis soon.

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