

A Comprehensive Review on Nephrolithiasis

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ABSTRACT

Nephrolithiasis is the term employed for kidney stones, also known as renal calculi. They are crystal concretions formed typically in the kidney. Calculi typically form in the kidneys and ideally leave the body via the urethra without pain. Larger stones are painful and may need surgical intervention. It is an increasing urological disorder of human health, affecting about 12% of the world population. The etiology of kidney stone is multifactorial. The most common type of kidney stone is calcium oxalate formed at Randall's plaque on the renal papillary surfaces. The mechanism of stone formation is a complex process which results from several physicochemical events including supersaturation, nucleation, growth, aggregation, and retention of urinary stone constituents within tubular cells. It is the most common disease of the urinary tract. The prevention of renal stone recurrence requires better understanding of the mechanisms involved in stone formation. Kidney stones have been associated with an increased risk of chronic kidney diseases, end – stage renal failure, cardiovascular diseases, diabetes, and hypertension. The symptoms of kidney stone are related to their location where it is in the kidney, ureter, or urinary bladder. Nephrolithiasis is responsible for 2 to 3 % of end – stage renal cases if it is associated with nephrocalcinosis. Therefore, this review has intended to provide a compiled up-to-date information on nephrolithiasis etiology, epidemiology, types and composition of kidney stone, pathophysiology, mechanism of renal stone formation, signs and symptoms, risk factors, complications, diagnosis and management of Nephrolithiasis.

KEY WORDS

Nephrolithiasis, Renal calculi, Calcium oxalate crystals, Percutaneous nephrolithotomy, Ureteroscopic lithotripsy.

I. INTRODUCTION

Kidney stone which is also called Renal calculus. A kidney stone is a firm, crystalline mineral material formed within the kidney [or] urinary tract become so huge as to impair usual renal function. There are certain circumstances where there is increase in the likelihood of stone formation, either by reduction in fluid volume [or] increase in mineral concentration can be enough to disappoint the delicate balance between the liquid and its solutes. An augment in mineral concentration in the kidneys may occur due to the metabolic changes [or] infections. Once a stone begins developing, it grows continuously due to the precipitation of urinary salts can form a clump of bacteria, degenerated tissue, sloughed-off cells, or a tiny blood clot etc, accumulate around the foreign particle and form encrust over it. As the stone size increases the surface available for mineral deposition increases constantly. Kidney stones are frequent cause of blood in the urine [Haematuria] and often severe pain the region of abdomen, flank, or groin. It has been observed that renal stones, are associated with systemic disease like Type 2 diabetes mellitus, obesity, dyslipidemia and hypertension. Life style and environmental factors contribute significantly in their formation. The condition of kidney stones is termed as Nephrolithiasis. Having stones in any location in the urinary tract is termed as Urolithiasis, and the term Ureterolithiasis is refers to stones situated in the ureters.

ETIOLOGY

Most patients with Nephrolithiasis form calcium stones [80%], most of which are composed primarily of calcium oxalate or calcium phosphate. The other main types include uric acid, struvite [Magnesium ammonium phosphate, and cystine

stones. Of note, one patient, may have a stone that contains more than one type of crystal.

EPIDEMIOLOGY

The prevalence and recurrence rates of nephrolithiasis are increasing, with limited options of effective drugs and procedures, affecting about 12% of the population worldwide. The incidence is estimated at 6,00,000 in the U.S. Between the ages of 20 to 49; kidney stones affect men more frequently than in women. The lifetime recurrence rate is higher in males than in females. This fact is attributed to the increasing incidence of obesity due to poor dietary habits and lack of physical activity.

COMPOSITION OF NEPHROLITHIASIS {KIDNEY STONE }

A kidney stone is a cluster of crystals when they are formed together to create a hard lump in one or both kidneys. They can vary in size from a few millimeters to several centimeters. The majority of stones will pass out of the body in the urine without any help, but some will require intervention to remove them. The urinary stone have been developed with the crystals of phosphate, uric acid, magnesium ammonium phosphate with apatite, and struvite. Among the urinary stones, calcium - containing stones have been found to about 75% of all urinary calculi, which may be present in the form of crystals of pure calcium oxalate [50%], calcium phosphate [5%] and a mixture of both compounds [45%]. The diet can effect the concentration of certain substances in the urine and can effect the acidity of urine. The 24 hour urine collection of urine may found in any of the given properties have increased risk of forming a stone:

1. High levels of calcium [Hypercalciuria]
2. High levels of oxalate [Hyperoxaluria]
3. High levels of Uric acid [Hyperuricaemia]
4. Low levels of Citrate [Hypocitraturia]

Calcium, Oxalate, Uric acid and Citrate are normal substances found in the blood. The acidity of any fluid are expressed as p H. The p H of less than 7 is called acidic, while p H greater than 7 is belongs to alkaline. Normal urine p H will vary during the day depending on diet and will usually range between 5 and 8. Calcium oxalate stones can be found in any p H of urine. The formation of uric acid stones is more acidic in urine while calcium phosphate stones form in more alkaline urine.

TYPES OF KIDNEY STONES

Most of the stones formed by calcium oxalate and is associated with hypercalciuria and hyperoxaluria.

- **Hypercalciuria:**

It is seen in conditions with high sodium diet, on loop diuretic therapy, renal tubular acidosis, sarcoidosis, cushing syndrome, aldosterone excess or condition associated with hypercalcemia.

- **Hyperoxaluria :**

It is seen in people with intestinal malabsorption syndromes (inflammatory bowel disease, pancreatitis) due to decreased secretion of intestinal oxalate and by binding of intestinal calcium in the bowel lumen increases the absorption of free oxalate and cause Hyperoxaluria.

- **CALCIUM OXALATE:**

This stones may form due to deficiency of urinary citrate an inhibitor of stone formation under metabolic acidosis, hyperuricosuria.

- **CALCIUM PHOSPHATE:**

This stones are very rare and tend to occur only in an abnormally high urinary p H.

- **STRUVITE:**

This stones are formed in collecting systems during infection with urea – splitting organisms. Struvite is one of the component present in staghorn calculi. Risk factors include UTI, Urinary catheters etc.

- **URIC ACID:**

About 5 – 10% of all stones are composed of uric acid. This is most commonly seen in people with obesity and other metabolic abnormalities may produce uric acid stones. They are most commonly seen in association with conditions that cause hyperuricosuria with or without hyper uricemia. This conditions are mainly seen in combination with disorders of acid/base metabolism where the p H of urine is excessively acidic which results in accumulation of uric acid crystals. The uric acid urolithiasis is done with the help of radiolucent stone with urice acidity which helps in diagnosis of uric acid crystals in the fresh urine sample.

- **CYSTINE STONE:**

People with certain rare inborn errors of metabolism have a tendency of crystal – forming substances in their urine. For example, people with cystinuria, cystinosis, and Fanconi syndrome may form stones composed of Cystine. Urine alkalisation

and dietary protein restriction are used to treat cystine stones.

• **XANTHINE STONE:**

People afflicted with xanthinuria often produces stones composed of Xanthine.

CLASSIFICATION OF KIDNEY STONES:

There are different kinds of renal stones and their correct identification is important in the selection of optimal treatment. The frequency of different stone type occurrence is shown in below table. Based on variations in mineral composition and pathogenesis, kidney stones are commonly classified into:

Composition	Causative	Factors Frequency (%)
Calcium Oxide, Phosphate, or both	Underlying metabolic abnormality Idiopathic (25%)	60 - 80
Struvite (triple Phosphate)	Infection	10 - 15
Uric acid	Hyperuricaemia and Hyperuricosuria Idiopathic (50%)	5 - 10
Cysteine	Renal tubular defect	1
Other (Xanthine, Indigo, triamterene, indinavir , etc.)		1

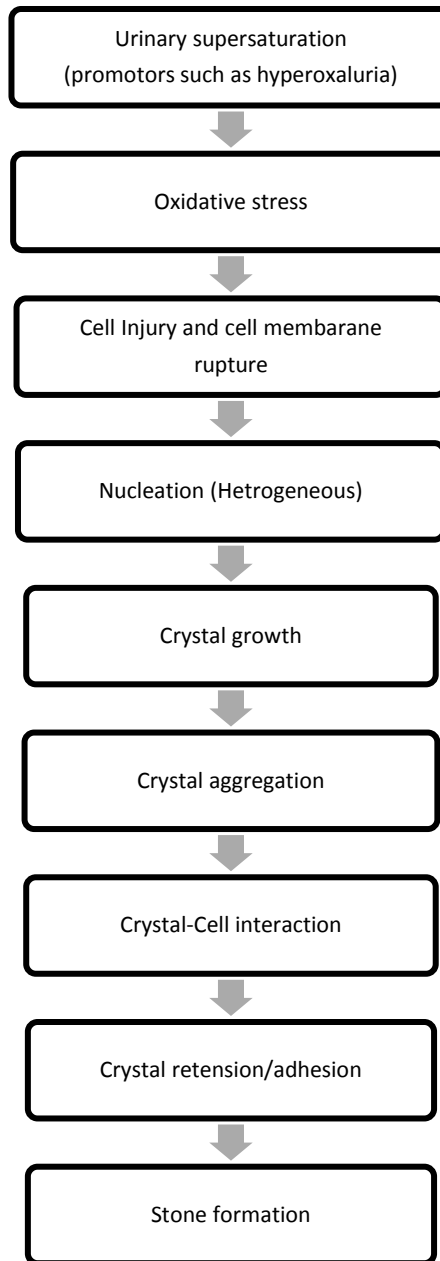
PATHOPHYSIOLOGY:

Renal stones are composed of insoluble salts from the urine and are formed by two basic mechanisms.

The first mechanism is the aggregaation of crystals with a non-crystalline protein (matrix) component. The salts in the urine precipitate and crystallise, aggregating the crystals, and causing them to grow into a mass sufficient to cause clinical symptoms.

In the second mechanism,which is mostly responsible for calcium oxalate stones,deposition of stone material occurs on a renal papillary calcium phosphate nidus ,typically a Randalls plaque (which always consists of calcium phosphate). The majority of stones are composed of mostly calcium salts,including those of calcium oxalate and calcium phosphate.Uric acid ,cystine and magesium ammonium phosphate (struvite) compose the remainder of the stones.

MECHANISMS OF RENAL STONE FORMATION:



Schematic representation of the various events of kidney stone formation

SIGNS AND SYMPTOMS:

Renal calculi are known to cause severe pain and symptoms of renal calculi may occur only when the stone begins to move towards the ureters. This severe pain is termed as renal colic, seen only on one side of your abdomen and in men, pain may radiate to the groin region.

Other symptoms renal calculi include:

- Vomiting

- Nausea
- Foul – smell urine.
- Chills
- Fever
- Frequent urination
- Blood in urine sample (red, pink, or brown urine)
- Urinating small amounts of urine.

- Discomfort in the side and back and below the ribs. This discomfort usually occurs only on the side of the renal calculi and does not cross over to the other side.
- Fluctuations in discomfort intensity, with periods of discomfort lasting 20 – 60 min.
- Discomfort waves radiating from the side and back to the lower abdomen and groin.
- Bloody, cloudy urine.
- Discomfort, pain, and inflammation on urination.
- Persistent urge to urinate.

In some cases, when the stone descends from the kidney into the ureters. Ureters are small, too delicate and too large to move down the ureter into the bladder. Passage of stones down through the ureters can cause spasms and irritation of the ureters can cause spasms and irritation of the ureters which causes blood to appear in the urine. In some cases stones obstruct the urine flow. It is said to be as urinary obstruction which can lead to kidney infection (pyelonephritis) and kidney damage.

RISK FACTORS:

Influenced by certain diseases, habits, composition of urine.

- Personal history of prior kidney stones increase the risk of kidney stones increase the risk of kidney stones by 15% within the first year, and 50% within the next ten years.
- A family history of kidney stones increase the risk by 2.5 times.
- Increased enteric oxalate absorption, typically due to malabsorption, leads to increased formation of calcium oxalate crystals.
- Urinary tract infections altering urinary pH in the setting of urease producing bacteria, producing struvite crystals.
- Low fluid intake.
- History of diabetes, obesity, gout, and hypertension.
- Acidic urine (pH < 5.5), which promotes uric acid formation in the setting of chronic diarrhea and gout.

COMPLICATIONS

Several complications can arise due to kidney stones, and subsequently, stones, that cause obstruction. These include:

- Abscess formation
- Urosepsis.

- Urinary fistula formation.
- Ureteral scarring and stenosis.
- Ureteral perforation
- Renal function loss due to long – standing obstruction.

DIAGNOSIS OF RENAL CALCULI:

Diagnostic test for renal calculus requires a complete urine examination, health assessment and a physical examination. Other tests include:

- Blood tests for calcium, phosphorus, uric acid and electrolytes etc.
- Blood urea nitrogen (BUN) and creatinine levels for assessing kidney functioning.
- Urinalysis to check for bacteria, blood, crystals, casts and white cells.
- Examination of stone type in determination of type renal calculi.

THE FOLLOWING TESTS CAN RULE OUT OBSTRUCTION:

ABDOMINAL X – RAYS:

An abdominal x- ray is a picture of the abdomen that uses low levels of radiation recorded on film or a computer. Abdominal x – rays is used to detect the location of kidney stones in the urinary tract. Not all types of stones are visible through abdominal x – ray.

ULTRASOUND OF THE KIDNEY:

Ultrasound is a non – invasive test used in diagnosing the renal calculi. By using sound waves we can detect kidney stones without exposure to radiation or to any contrast dye. Ureteral stones cannot be detected by using ultrasound, unless the stone is situated at the junction of the ureters and the bladder.

MRI OF THE ABDOMEN AND KIDNEYS:

Magnetic Resonance Imaging (MRI) is a test done with the help of a magnetic field and radio wave energy to make images of organs and structures inside the abdomen. When compared to x – ray, ultrasound and MRI ultrasound gives the complete information regarding the presence of stones.

INTRAVENOUS PYELOGRAM (IVP):

In this diagnostic test done with the help of a dye injected intravenously. This dye is relatively dense and is excreted through the kidneys and can be diagnosed by using x – rays. The dye is excreted through the kidneys appears in the collecting ducts and then moves down into the ureters. In the presence of blockage it takes long time for the dye

to be excreted. IVP is a reliable test for Renal / Ureteral stones, but it has a few drawbacks like radiation exposure, intravenous dye may cause some adverse reaction. Intravenous pyelogram is not a reliable test to diagnose other conditions.

RETROGRADE PYELOGRAM:

The retrograde pyelogram is a diagnostic test done with the help of a dye to find out obstruction in the urinary tract. During this test, a thin tube (Cystoscopy) into the urethra, which carries urine out of the body through bladder. Physician will then put a catheter through the cystoscope and into a ureter. Dye is injected with the help of catheter, and x – rays imaging technique should be used.

TREATMENT:

NON PHARMACOLOGICAL TREATMENT :

- By increasing fluid intake for more than 2 litres per day.
- Increasing citric acid intake.
- Moderate intake of calcium.
- Limited sodium intake.
- Avoiding supplemental vitamin C.
- Avoiding oxalate rich foods.
- Limiting animal protein.
- Limited consumption of soft drinks containing phosphoric acid.
- Magnesium intake reduce the symptomatic effect of nephrolithiasis.

PHARMACOLOGICAL TREATMENT:

SMALL STONES:

The small stones do not require much treatment; they get off the body by drinking précised amount of water. Drinking plenty of water to about 4 – 5 lit / day helps to get rid of stones throughout the body through urine. The movement of stones creates pain; the moving pain can be treated with certain pain relievers.

MEDICAL THERAPY FOR KIDNEY STONES:

Usually doctors prescribe with alpha blockers; they relax the muscles in the ureters, which help to pass the kidney stone more quickly. Diuretics are also useful for increasing the urine flow to pull out the stone.

LARGE STONES:

Large stones are not easy to remove by drinking plenty of water they cannot pass out from the body due to stuck in the renal tube. These stones may harmful for body because they can damage the kidneys and cause internal bleeding, loss of nephron or easy to get infected with some urinary tract infections. The larger stones cannot pass throughout from the kidneys because they are large in shape and are may be chances of break down. They also cause bleeding, UTIs and damage in kidneys.

MEDICAL EXPULSIVE THERAPY :

DIURETICS

DRUG	DOSE	MECHANISM OF ACTION	USES	ADVERSE EFFECTS
chlorthalidone	25mg per day	These drugs inhibits formation of calcium stones by inhibiting urinary calcium excretion.	Kidney problems Hypertension Strokes	Black tarry stools Bleeding gums Chest pain

ALLOPURINOL

Allopurinol	200mg orally O.D	Inhibits the uric acid crystals formation by interfering with the uric acid production in liver	Renal calculi Gout	Rash Hives Diarrhea Nausea Vomiting
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CALCIUM CHANNEL BLOCKERS

Nifedipine	90mg	Relaxes smooth muscle cells by blocking calcium channels	Renal calculi Hypertension Angina	Muscle cramps Bloating
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ALPHA BLOCKERS

Tamsulosin	0.4mg	Relaxes the smooth muscles by antagonism on the alpha 1 receptor	Benign Prostatic Hyperplasia Kidney stones	Floppy iris syndrome Severe hypotension
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NEPHROLITHOTOMY:

If the doctors find the large stones in or near kidneys the Nephrolithotomy is one of the options. During this surgery the patient receives general anesthesia. The device contains a thin telescopic instrument which removes the kidney stones which is more than in 2 cm in size. This instrument is better used for the stones near the pelvic region.

Urine Alkalization :

Dietary elements that alkalinize the urine include sodium bicarbonate, potassium citrate, magnesium citrate and potassium citrate (a combination of sodium citrate dehydrate and citric acid monohydrate). Increasing the urine pH to 6.5 which aids in dissolution of uric acid stones. Increasing the urine pH > 7.0 increase the risk for the formation of calcium phosphate stone. Testing with Nitrazine paper periodically to ensure the urine pH remain in the optimal range.

TREATMENT:

Management of pain often requires intravenous administration of NSAIDs or opioid (e.g. Tramadol). Oral medications are less effective. Medical expulsive therapy aid guide appropriate use of drugs for treatment of renal calculi.

LITHOTRIPSY:

Extracorporeal shock wave lithotripsy (ESWL). It is a non-invasive technique used to remove calculus near renal pelvis.

Mechanism :

ESWL is carried out with the help of a lithotripter machine to deliver externally high-intensity pulses of Ultrasonic energy used to break the stone into fragments over a period of about 30-60 minutes.

Uses :

It is used in the treatment of normal stones located in the region of kidney and upper ureter which increase the risk of stone formation (stone size and

number) not less than 20mm (0.8 in) and kidney with normal anatomy. For a stone of about > 10mm (0.4 in), ESWL is helpless in case of fragmentation of stone in one treatment, two or three treatments may be needed.

Factors Effecting :

There are number of factors can influence its efficacy, chemical composition of the stone and the exact location of the calculi in the kidney, hydronephrosis and body mass index.

Adverse Effects :

Commonly seen adverse effects of ESWL are acute trauma, such as bruising at the site of shock and damage to blood vessels present in the kidney. ESWL – induced acute kidney injury is dose – dependent and can be severe, including internal bleeding and sub capsular hematomas. On rare occasions some patients may require blood transfusion and even leads to acute renal failure.

URETEROSCOPY :

It is used for complete examination of upper urinary tract, performed with the help of Ureteroscopic that is passed through the urethra and the urinary bladder, and then finally into the ureter. This procedure is useful in the diagnosis and treatment of disorders such as renal calculi. The small stones can be removed in one piece and bigger ones are usually broken before the removal during Ureteroscopic.

II. CONCLUSION:

Prevention is always better than cure. Dietary habits play an important role in formation of renal calculi. Preventive measures are dietary changes along with some medications. Current precautions to reduce the risk of renal calculi include : Increasing citric acid intake, increasing total fluid intake to > 2 litres per day, moderate calcium intake, limiting sodium intake, avoidance of high doses of vitamin C, less intake of animal protein not > 2 meals daily, limited intake of soft drinks, < 1 litre of soft drink per week. Citrate reduce the risk of calcium oxalate type of renal calculi. By following these preventive measures we can reduce renal calculi.

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