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UROLITHIASIS: TYPES, MECHANISM, DIAGNOSIS & HERBAL TREATMENT

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Abstract: A kidney stone is a solid concretion or crystal aggregation generated in the kidneys from dietary minerals in the urine. It is also known as a renal calculus or nephrolithiasis. Stone formation in the kidney is one of the oldest and most widely spread diseases known to man. It is one of the most common and painful urologic disorder of the urinary tract that affects millions of people every year. The life time risk of developing lithiasis ranges between 10-12% and significantly affects the economy and public health as it has a high rate of recurrence. In general, the probability of creating stones varies around the globe and is estimated to be 1–5% in Asia, 5–9% in Europe, and 13% in North America. In a period of 20 years, renal stones have a 75 percent recurrence rate. Urinary lithiasis is generally the result of an imbalance between inhibitors and promoters in the kidney. Approximately 85% of the stones in humans are calcium stones comprising oxalate and phosphate, either alone or combined. Urinary supersaturation and crystallization, Crystal nucleation, Crystal growth, Crystal aggregation these mechanism are responsible for formation of kidney stones. There are also some genetic factors and systemic factors that involved in the formation of stones like Idiopathic hypercalciuria and hyperoxalosis & inflammatory disorders respectively.

Index Terms - Urolithiasis, struvite stones, Urinary supersaturation, hyperoxalosis, Idiopathic hypercalciuria.

I. INTRODUCTION

A kidney stone is a solid concretion or crystal aggregation generated in the kidneys from dietary minerals in the urine. It is also known as a renal calculus or nephrolithiasis (Zaidi et al 2006). Urinary calculi are becoming more common over the world, with calcium oxalate (CaOx, CaC2O4) being the most common component, followed by struvite, cystine, uric acid, and other chemicals (Trinchieri et al, 2006). In general, the probability of creating stones varies around the globe and is estimated to be 1–5% in Asia, 5–9% in Europe, and 13% in North America. In a period of 20 years, renal stones have a 75 percent recurrence rate. Stone formation has several known etiological causes, including inherited, nutritional, geographic, and infectious disorders (Abbagani et al, 2010). The likelihood of recurrence is high—more than 50%. About 80% of kidney stone cases are calcium-containing stones, which commonly comprise calcium oxalate (CaOx), either by itself or in conjunction with calcium phosphate. There are two types of calcium oxalate stones: calcium oxalate monohydrate (COM) and calcium oxalate dihydrate (COD) (Niramaladevi et al, 2014). There are several steps involved in the pathophysiology of calcium oxalate stone development (khare et al 2014). Increased urine supersaturation triggers the crystallisation of the stone, which is followed by the production of solid crystalline particles inside the urinary system. The process of nucleation, in which salts

that can cause kidney stones aggregate into clusters in a supersaturated urine solution, occurs next (Basavaraj *et al*, 2007). These crystals eventually become retained and collect in the kidney after they develop and combine with other crystals in solution (Kok *et al*, 1990).

Typically made of calcium oxalate monohydrate, calcium oxalate dihydrate, calcium phosphates, uric acid, other organic substances like urates, cystine, etc., organic debris, or a combination of two or more of the aforementioned ingredients, renal stones are solid concretions that form within the upper urinary tract (khare et al 2014). With the exception of organic detritus, these substances must convert from liquid to solid throughout the upper urinary tract (urine). The so-called supersaturation of urine with regard to the component in issue, or the fact that urine contains more dissolved substance, is therefore a necessary condition for stone formation.

With the exception of organic detritus, these substances must convert from liquid to solid throughout the upper urinary tract (urine). The so-called supersaturation of urine with regard to the component in question, or the presence of an excess of dissolved chemical that either spontaneously releases as new solid particles or is gradually depleted by the growth of existing crystals, is therefore a requirement for stone formation.

The likelihood of developing calcium oxalate stones rises with age and is triggered by the attachment of a crystal to the surface of renal tubular epithelial cells. Although the majority of the crystals that develop in the renal tubules' cavities are excreted in the urine in healthy individuals. It is believed that macrophages and/or lysosomes within cells digest crystals that adhere to the surface of renal tubular epithelial cells. However, renal tubular cells are damaged in people with hyperoxaluria or crystal urine and crystals are easily attracted to them. Renal tubular cell damage is thought to be caused by a variety of reasons. Crystal-cell interaction occurs when crystals on the surface of renal tubular cells enter the cells. The crystal and crystal aggregates continue to grow until a stone is eventually created. Urolithiasis brought on by calcium oxalate (CaOx) stones affects more than 60% of patients with renal stones. Even though urolithiasis has been there since ancient times, many experts are still working to understand how CaOx kidney stones originate. There is ongoing debate over the physiochemical processes that lead to stone formation in urine through the precipitation, growth, aggregation, and concretion of different lithogenic salts. The interaction between crystals and renal tubular epithelial cells, particularly the adherence or endocytosis of crystals by cells, has also lately received attention from certain researchers as a key element in the development of stones. 1–3 Furthermore, some studies have demonstrated that pre-existing cell injury makes renal tubular epithelial cell harm in crystal-cell interactions more likely to happen. Nearly all urine is supersaturated with calcium oxalate hydrates, and less commonly with other molecules including uric acid and other kinds of calcium phosphate. Oxalocalcic stones should therefore be the most common kind of calculi. In actuality, calcium oxalate is the primary component in about 80% of all stones. When the normal urine composition or acidity (pH) is appropriately modified due to things like a change in food, diuresis, etc., other compounds, which frequently accompany the main component, are generated. Additionally, the fact that pee is supersaturated suggests that all urine has a natural tendency to form solid particles. Renal lithiasis should be more common than it is because calculi are typically concretions of solid particles joined together in some way. Therefore, the question of why just a small portion of the population is susceptible to stone production emerges. The solution is based on the notion that urolithiasis is a multifactorial phenomenon that can only

manifest when all necessary conditions are met at once. With a roughly one in ten lifetime risk in the general population, kidney stones are one of the most excruciating medical illnesses to ever affect a human being. Numerous epidemiologic studies indicate that over the past 35 years, there has been a sharp rise in the prevalence of stone disease. It's significant that it primarily affects productive young people, with incidence peaked in the third and fourth decades of life. The likelihood of recurrence is relatively high, which lowers these people's productivity. Zaidi *et al*, 2006.

2. TYPES OF KIDNEY STONES:

Kidney stones are made up of calcium oxalate and calcium phosphate in about 70–80% of cases. Less than 1% of the remaining stones are cystine- or drug-related-stones, and 10% of the rest are made of struvite and 10% of uric acid. Men are more likely to develop calcium and uric acid stones than women are to develop struvite stones.

a) **Calcium stones**: Calcium oxalate makes up the majority of calcium stones, whether they are formed on their own or, considerably more frequently, in conjunction with calcium phosphate or calcium urate. Calcium stones can form as a result of hypercalciuria, low urine volume, and hypocitraturia. Diseases including hyperparathyroidism, cancer, sarcoidosis, and excess vitamin D are among those that frequently co-occur with hypercalciuria. "Idiopathic hypercalciuria" is the term for hypercalciuria that has no other known cause. Although there are certain uncommon monogenic causes of hypercalciuria and kidney stones, such as Dent's disease, an X-linked condition characterised by hypercalciuria, nephrocalcinosis, and the onset of renal failure, familial idiopathic hypercalciuria is likely a polygenic feature. A risk factor for the development of calcium phosphate stones is alkaline urine. Another danger sign for calcium Hyperoxaluria, often known as oxalate stones, is brought on by intestinal disorders (enteric hyperoxaluria) hereditary oxalate metabolism issues (primary hyperoxaluria). Dietary oxalate may have a role in the formation of stones; in particular, oxalate-rich foods like spinach, beets, and rhubarb may increase urinary oxalate excretion and raise the risk of calcium oxalate stones. Ascorbic acid, a component of vitamin C, is digested, which can result in increased oxalate production during high dose vitamin C therapy. A risk factor for the development of calcium phosphate stones is alkaline urine. Another danger sign for calcium Hyperoxaluria, often known as oxalate stones, is brought on by intestinal disorders (enteric hyperoxaluria) hereditary oxalate metabolism issues (primary hyperoxaluria). Dietary oxalate may have a role in the formation of stones; in particular, oxalate-rich foods like spinach, beets, and rhubarb may increase urinary oxalate excretion and raise the risk of calcium oxalate stones. Ascorbic acid, a component of vitamin C, is digested, which can result in increased oxalate production during high dose vitamin C therapy.

b) Uric acid stones: Pure uric acid calculi are radiolucent on plain radiographs but visibleon ultrasonography or computerized tomography (CT). These stones tend to form in individuals with hyperuricosuria. Approximately 15-20% of patients with uric acid stones have a history of gout. A diet rich in animal protein, because of its high purine content, which produces uric acid in its catabolism, may increase the risk of uric acid stone formation. At a urinary pH of less than 5.5, uric acid is poorly soluble, but solubility increases at a pH greater than 6.5. Cystine stones These stones tend to form only in patients with cystinuria, an autosomal recessive disorder affecting 1 in 15,000 adults in the USA that accounts for

only 1% of patients with nephrolithias. Cystinuria occurs equally in males and females, although males are more severely affected. Stones begin to form in the 1st to 4th decades of life and tend to be large, multiple and bilateral. The diagnosis can be made by finding typical hexagonal crystals in the urine. Urinary tract infection and obstruction are common, as is stone recurrence every 1-4 years (Pearle *et al*, 2006).

c) Struvite stones: Struvite stones are also called triple phosphate stones, or infectionstones. They form in the presence of upper urinary tract infections with urease-producing bacteria (most commonly Proteus and Klebsiella). Normal urine is under saturated with ammonium phosphate; struvite stone formation occurs only when ammonia production is increased and the urine pH is elevated, which decreases the solubility of phosphate. Bacterial urease is essential for the development of struvite stones because it leads to an elevation in ammonium, carbonate and urinary pH all at the same time. In this setting phosphate combines with ammonium, magnesium and carbonate to form a stone composed of magnesium ammonium phosphate (struvite) and calcium carbonate.

d) Cystine stones: Cystine stones are rare and hereditary; they look more like crystals thanstones. Cystine stones are produced in patients with a homozygous recessive gene for cystine transport, producing excess urinary cystine. Cystine is an amino acid of cysteine-S-S-cysteine. (The four dibasic amino acids are cystine, ornithine, lysine, and arginine, hence the mnemonic: COLA.) Normal individuals generally excrete into urine <100 mg cystine/day whereas the majority of homozygous cytinurics excrete > 200 mg/day. There are no known inhibitors of cystine. Cystine is more soluble at a pH of 9.6 and higher compared to lower PHs, but it is practically impossible to achieve such a high urine pH by oral alkali agents (and not without risk of calcium phosphate stone formation). Urease breaks down urinary urea into ammonia and carbon dioxide: Urea → 2NH3 + CO2 The ammonia produced by this reaction then combines with water: NH3 + H2O → $NH4^{+}$ + OH^{-}

Resulting in increased availability of ammonium in alkaline urine. Struvite stones commonly urinary tract anatomy, or require frequent bladder catheterization. The stones may also occurs

on infected calcium, uric acid or cystine stones, especially after instrumental procedures. Struvite stones are three times more common in women than men, presumably because urinary tract infections are more common in women. They are typically very large and may be so large as to fill the renal pelvis (Asplin *et al*, 1998).

3. MECHANISM OF STONE FORMATION

1.Urinary supersaturation and crystallization: Supersaturation of Urinarysupersaturation is the driving force behind crystal formation in the kidneys. Since formation of crystalline particles start from supersaturation. In tubular fluid and urine, crystallization processes are largely dependent on solution composition. A variety of urinary constituents may affect solution . For instance, by forming soluble complexes with calcium and oxalate, respectively, citrate and magnesium reduce free ion activity and the relative calcium oxalate (Khan SR *et al*,1996).

2.Crystal nucleation: The initial step in the transformation from a liquid to a solid phase in a supersaturated solution is called nucleation. This process begins with coalescence of stone salts in solution into loose clusters that may Increase in size by addition of new components.

3.Crystal growth: Once a crystal nucleus has achieved a critical size and relativesupersaturation remains above 1, overall free energy is decreased by adding new crystal components to the nucleus. This process is called crystal growth. Crystal growth is one of the prerequisites for particle formation.

4.Crystal aggregation: The process whereby crystals in solution stick together to form larger particles is called aggregation. Some researchers have proposed that crystal aggregation is the most important step in stone formation. Although crystal growth is definitely a step in CaOx renal stone formation the process of growth is so slow that crystals cannot become large enough to obstruct the renal tubules and be retained there by this mechanism alone, as several minutes are required for the tubular fluid to pass through the kidney (Tsujihata *et al*, 2008).

Table no.1: Risk factors of kidney stones:

Hereditary and other disease related			**Environment**
Genetic	Idiopathic hypercalciuria Hyperoxalosis Cystinuria: Dent's disease	Climate	Heat Water loss, sweating
Kidney disease related	Medullary sponge kidney PKD (10% develop stones) Horse shoe Metabolic hypercalcemia, hyperparathyroidism, DM and obesity		
Systemic disease	GI, inflammatory bowel disease		
Hyperparathyroidism	CaP stone		

4. CLINICAL DIAGNOSIS OF KIDNEY STONES

Non-obstructing kidney stones produce no symptoms or signs apart from hematuria. However, the kidney stone may cause severe pain, usually accompanied by nausea, vomiting and hematuria (renal colic) when it passes into the ureter. Patients may also complain of urinary frequency and urgency. These signs and symptoms lead to many emergency department visits and hospitalization. The pattern of the pain from stone depends on its location: a stone in the upper ureter leads to pain in the flank that may radiate to the upper abdomen. When the stone is in the lower ureter, pain may radiate to the ipsilateral testicle in men or labium in women. If the stone is lodged at the uretero vesical junction, the main symptoms will be urinary frequency or urgency. Symptoms quickly improve after passing the stone. On physical examination, the patient is often in excruciating pain, and is unable to achieve a comfortable position. Ipsilateral

costovertebral angle tenderness may also be present. Laboratory tests may show a leukocytosis which may be due to a stress response or infection. Serum creatinine is often elevated if the patient is volume depleted, or if there is bilateral ureteral obstruction or unilateral obstruction in a patient with a solitary kidney. The urinalysis will have red blood cells, white blood cells and occasionally crystals. However, because of the often non-specific physical examination and laboratory findings, imaging studies are critical in making the diagnosis. Initial evaluation includes obtaining a non-contrast helical CT, which can accurately visualize the size and location of the stones. A kidney, ureter and bladder (KUB) film, although it is insensitive to uric acid stones since they are radiolucent and therefore are not visualized. However, it can visualize calcium – containing, struvite and cystine stones in the kidney or ureter. Complete ureteral obstruction and upper urinary tract infection (UTI) are indications for stone removal by extracorporeal shock wave lithotripsy (ESWL) or surgery (Fakheri *et al*, 2009).

5.MEDICAL AND NUTRITION EVALUATION OF KIDNEY STONES

A comprehensive history should be taken by one of the health care providers, and the following items should be covered: prior kidney stones, composition of prior stones if known, dietary history including an estimate of typical daily fluid intake, social history including details regarding occupation and lifestyle, and family history. The medical history should focus on identifying diseases that increase stone risk including conditions that lead to hypercalciuria, gout, chronic diarrhoea and malabsorptive gastrointestinal disorders (Parks *et al*, 2002).

Table no.2: Herbal plant used in kidney stones:

S.No.	Name of Herbal plant	Family	uses
1	*Aerva javanica*	Amaranthaceae	Herb Diuretic, Purgative, Demulcent
2	Aerva lanata	Amaranthaceae	Cough, Sore throat, Diabetes, Lithiasis
3	*Ammannia baccifera*	Lythraceae	Ringworm, Parasitic skin affection, Anti-typhoid, Anti-tubercular properties
4	*Arctostaphylos ura ursi*	Asteraceaer	Diuretic, Diaphoretic, Gout, Skin affection
5	*Ascyrum hypericoides*	Asclepidaceae	Emetic and Cathartic
6	*Asparagus racemosus*	Liliaceae	Herb tonic, Diuretic, Galactagogue
7	*Berginia ligulata*	Saxifragaceae	Astringent. Diuretic, Lithontriptic
8	*Bridolia montana*	Euphobiaceae	Bark Astringent, Anthelminetic
9	*Caesalpinia huga*	caesalpinioceae	Root Diuretic, Lithontriptic
10	*Celosia argentla*	Amararanthaceae	Diarrhoea, Eye troubles, Sore mouth
11	*Chelidonium majus*	Papaveraceae	Diuretic, Antispasmodic, bitter
12	*Chimaphila numbellata*	Cruciferae	Diuretic, Expectorant, Stimulant
13	*Desmodium styracifolium*	Papilionaceae	Roots Emmenagogue, Stomachic
14	*Didymocarpus pedicellata*	Gesneriaceae	Leaves Lithontriptic

15	*Dolichos biflorus*	Leguminoceae	Diuretic, Astringent, Tonic
16	*Mentha piperita*	Labiatae	Spasmolytic, Carminatives, Febrifuge, Nausea

(Chitme *et al*,2010)

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