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AN OVERVIEW OF UROLITHIASIS

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Abstract

Urolithiasis is the term for the condition in which stones develop in the kidney, bladder, and/or urethra (urinary tract). Men are twice as likely as women to develop stones. Anguish that extends from the flank to the groin or to the genital area and inner thigh is a defining feature of stones that block the ureter or renal pelvis. The name of the stone kind comes from the minerals that make it up. Struvite (magnesium ammonium phosphate), calcium oxalate, urate, cystine, and silica are the most frequently occurring stones. In the world, calcium is present in the most prevalent kind of kidney stones. Preventive actions vary according on the kind of stones. elevated danger of renal failure. Randall's plaque, which forms on the renal papillary surfaces, is the most prevalent site of calcium oxalate stone development. The nucleation, crystal development, aggregation, and retention of urine stone ingredients within the kidney are the mechanisms involved in the creation of stones.

Keywords: Urolithiasis [kidney stones], Calculi, struvite, Calcium oxalate, Urate.

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Introduction

The formation of stone in the urinary system, i.e. in the kidney, ureter, and urinary bladder or in the urethra is called urolithiasis. 'Urolithiasis'. Urolithiasis is one of the major diseases of the urinary tract and is a major source of morbidity. Stone formation is one of the painful urologic disorders that occur in approximately 12% of the global population and its re- occurrence rate in males is 70-81% and 47-60% in female. It is assessed that at least 10% of the population in industrialized part of the world are suffering with the problem of urinary stoneformation. The occurrence of the renal calculi is less in the southern part when compared withother parts. The rate of occurrence is three times higher in men than women, because of enhancing capacity of testosterone and inhibiting capacity of oestrogen in stone formation. It has been found that the formation of urinary calculi dates back not only to 4000 B.C in the tombs of Egyptian mummies also in graves of North American Indians from 1500 to1000 B.C. Stone formation is also documented in the early Sanskrit documents during 3000 and 2000 B.C.

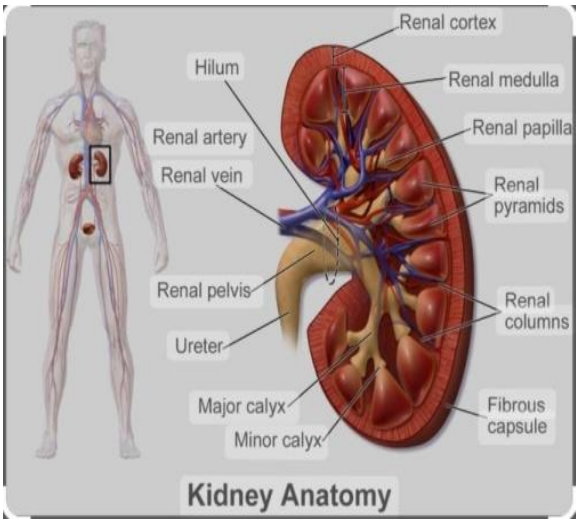


Figure:1

Epidemiology of kidney Stones:

Urolithiasis affects about 12% of the world population in their lifetime and at a certain stage. It affects all ages, sexes and races, but occur more often than in men than in women between certain ages of 20 and 49. If patients can not apply the remission rate of secondary stone formations is reported at 10–23% per year, 50% in 5–10 years and 75% in 20 decades ofthe patient [3]. and it is estimated that every year 600,000 Americans are suffering from urinary stones. In the Indian population, approximately 12% of them will be projected to have urinary stones and 50% of them may end up with renal function failure.

Types of Kidneys Stones:

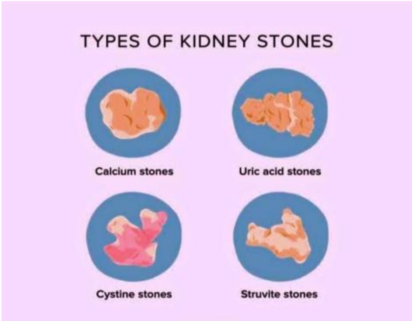


Figure:2

1) Calcium Stone:

stones are predominant renal stones comprising about 80% of all urinary calculi, Calcium oxalates stone are crystalline component of calcium oxalate monohydrate, calcium oxalate dihydrate and calcium oxalate trihydrate.

Symptoms:

A kidney stone may not cause symptoms until it moves around within your kidney or passes into your ureter the tube connecting the kidney and bladder. At that point,you may experience these signs and symptoms:

- Severe pain in the side and back, below the ribs
- Pain that radiates to the lower abdomen and groin
- Pain that comes in waves and fluctuates in intensity
- Pain on urination
- Pink, red or brown urine

2) Uric Acid Stones:

Uric acid stone is a crystalline component of uric acid anhydrous and uric acid dehydrate, with uric acid stone usually affecting5-10% of the analyses population of renal stone. Uric acid is a metabolic product and gout disorder also affects about 25 percent of patients with this block. Low urine volume, hyperuricosuria and acid urine pH (pH < 5.05) arethe main reasons for this

3) Cystine Stones:

Cystine stone is caused by cystine in the urine due to high levels of essential amino acid. Cystine stone usually occurs in childhood and is a rare hereditary metabolic disorder thataffects 1-3% of the studied kidney stone population.

Symptoms:

- Pain while urinating
- Blood in the urine
- Sharp pain in the side or the back (almost alwayson one side)
- Pain near the groin, pelvis, or abdomen
- Nausea and vomiting

4) Struvite Stones:

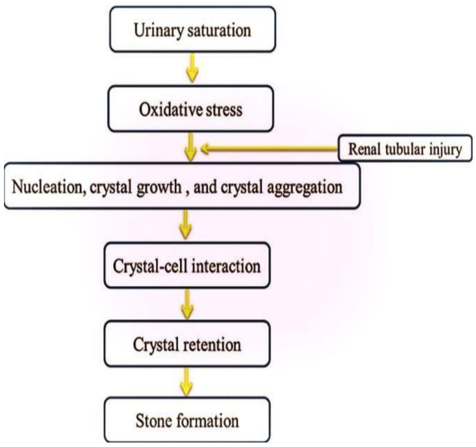
Struvite stone is an infectious urinary stone of hexahydrate or struvite ammonium magnesium phosphate. It is a fascinating inorganic mineral of phosphate closely associated with chronic urinary tract infection due to certain microorganisms such as bacteria causing urease. The bacterium transforms urea into ammonium in combination with magnesium and phosphate. Phosphate is less soluble in alkaline than in acidic pH, so phosphate precipitates on to the in soluble ammonium products, yielding to a large stag horn stone formation.

Inhibitors of Stones formation:

Normal urine contains chelating agents such as citrate that inhibit the nucleation, growth and aggregation of calcium containing crystals. Other endogenous inhibitors include calgranulin (an S-100 calcium binding protein), TammHorsfall protein, glycosaminoglycans, uropontin (a form of osteopenia), nephrocalcin (an acidic glycoprotein), prothrombin F1 peptide, and bikunin (uronic acid-rich protein). The biochemical mechanisms of action of these substances have not yet been thoroughly elucidated. However, when these substances fall below their normal proportions, stones can form from an aggregation of crystals. Kidney stones often result from a combination of factors, rather than a single, well-defined cause. Stones are more common in people whose diet is very high in animal protein or who do not consume enough water or calcium. They can result from an underlying metabolic condition, such as distal renal tubular acidosis, Dent's disease, hyperparathyroidism, primary hyperoxaluria or medullary sponge kidney. In fact, studies show about 3% to 20% of people who form kidney stones have medullary sponge kidney. Kidney stones are also more common in people with Crohn's disease. People with recurrent kidney stones are often screened for these disorders. This is typically done with a 24-hour urine collection that is chemically analyze for deficiencies and excesses that promote stone formation.

Mechanism of Action

Stone forming processes include nucleation of stone constituent crystals, their growth or accumulation to a size that may interfere with some intrarenal structure, persistence within the collection system of the kidney or renal, and further aggregation and/or secondary nucleation to form the clinical stone.



Fig;3 Mechanism of Action

Nucleation;

Nucleation is the method of associating free ions into microscopic particles in the solution. Crystallization can occur in microenvironments of solution, as can occur at certain points in the nephron, as well as on surfaces such as cells and extracellular matrix. There is considerable controversy over the value of free solution crystallization versus crystallization atother locations, in renal tubules or on bladder walls, in normal or ceareas denuded by certain types of injury, or in interstitial.

1. Crystal Growth:

Microscopic crystal growth is accomplished by transferring ions out of solution to the growing crystal. While some growth of nuclear crystals must occur through the

movement of ions from solution, this is clearly a limited process, since giant single crystals of stone constituents are generally not observed. Stone growth is more likely to be accomplished by aggregating preformed crystals or secondary crystal nucleation on another's matrix-coated layer. It has been suggested that the development of these microscopic crystals cannot occur without aggregation or attachment to intra renal structures to the degree that they can be maintained in the kidney on the basis of size alone. It has been proposed that the growth of these microscopic crystals to the extent that they can be retained in the kidney on the basis of size alone cannot occur without aggregation or attachment to specific intra renal structure.

Aggregation:

Aggregation is a process through which crystals are agglomerated that form into larger multicomponent particles in a free solution It may also include the secondary nucleation phenomenon of new crystals on the surface of those already formed. Stones are an accumulation of crystals and an organic matrix, which is the binding agent. The organic matrix includes proteins, lipids, polysaccharides and other substances derived from cells.

Cell Interaction crystal and formulation;

The attachment of grown crystals to the renal tubular lining of epithelial cells is referred to as crystal retention or contact between crystal cells. Renal tubular epithelial cells were injured inindividuals with hyperoxaluria due to exposure to high concentrations of oxalates or sharp crystals of calcium oxalate monohydrate (COM). Crystal cell contact results in the passage of crystals to the basement membrane from the basolateral side of the cells. COM crystal's contactwith the renal epithelial cell surface could be a crucial initiating activity in nephrolithiasis.

Cell Injury and Apoptosis

Exposure to high oxalate or CaOx crystals contributes to epithelial cell damage, which is a predisposing factor for the subsequent formation of stone. CaOx crystal deposits in the kidneys up regulate the macromolecules expression and synthesis that can promote inflammation. Crystals can be transported to or endocytized by cells. Injured cells have been suggested to develop a nidus that promotes particle retention on the renal papillary surface.

Randalls plaques[(5)]:

While urine is not generally supersaturated with respect to calcium phosphate, such conditions may exist in Henle's loop. This may result in calcium phosphate precipitation in the inner medulla at interstitial sites. These deposits often become large enough in the form of Randall'sPlaques to be visible macroscopically. Such deposits have been suggested to serve as a nidus for the production of the most common variety of calcium oxalate stones. Several studies haveshown that stones tend to have been directly attached to the plaque of the Randall's which has eroded on the surface of a renal papilla through the overlying uroepithelium. Although Randall's plaques appear to be a risk factor for stone formation, it is still uncertain whether they are required in any forming stone, as both intra tubular crystals and prominent crystalluria

are characteristics of stone disease. Urine blockers include small organic anions like citrate, small inorganic anions like pyrophosphates, multivalent metal cations like magnesium, or macromolecules like osteopontin glycosaminoglycans, glycoproteins, urinary tract. prothrombin fragment-1, and proteins of Tamm – Horsfall.

Diagnostic Managing ultrasound:

Many imaging modalities can be useful in diagnosing urolithiasis, including US; conventional radiographs of the kidney, ureter and bladder (KUB); non-contrast CT; and magnetic resonance(MR) urography [7]. Unlike in the adult population, where non-contrast CT is considered the gold standard in the diagnosis of urolithiasis, US, being a non-ionizing, easily accessible besides procedure, is recommended as the initial diagnostic method in children [1,6,10]. Although sensitivity and specifcity of US depend on the physician as well as the machine and patient position, they have been reported to be as high as 67–90% and 95–100%, respectively [1, 11].

structure in the bladder.

Kidney, Ureter, Bladder (KUB) Radiography:

Kidney, ureter and bladder (KUB) radiography applied alonehas low estimated sensitivity andspecificity (57–69% and 76–82%, respectively) Calculi may be obscured bybowel content due to inadequate bowel preparation, obesity or extrarenal calcifications. Moreover, not all stonesare radiopaque. Visibility of a stone on a KUB radiograph depends on its compositioncalcium-containing calculi are radiopaque; struvite or cystine are sometimes opaque; uric acid, medication or matrix stones are radiolucent and impossible to see on radiography .Exact location orsigns of pelvicalyceal dilatation are undetectable on KUB radiographs.

NON- Contrast Computed Tomography:

Non-contrast CT is considered the gold standard for the diagnosis of urolithiasis in adults .It has the potential to visualize almost all types of calculi, even those located in the ureters; to define the exact localisation, size and shapeof stones; and to reveal signs of pelvicalyceal dilatation or possible differential diagnoses Given all these and its very high sensitivity (97– 100%) and specific(96–100%) in diagnosing urolithiasis, non-contrast CT would be considered the perfect method if not for its radiation burden .

Causes of Urolithiasis:

Dietary factors that increase the risk of stone formation include low fluid intake and high dietary intake of animal protein, sodium, refined sugars, fructose and high fructose corn syrup24, oxalate19, grapefruit juice, apple juice, and cola drinks. Stone formation commonly occur due to inadequate urinary drainage, foreign bodies in urinary tract, microbial infections, diet with excess oxalates and calcium, vitamin abnormalities like vitamin A deficiencies excess vitamin D, and metabolic diseases like hyperthyroidism, cystinuria, gout, intestinal sunction etc. [3] Calcium oxalate is considered as main constituent in the renal calculi.

Calcium:

Calcium is one component of the most common type of human kidney stones, calciumoxalate. Unlike supplemental calcium, high intakes of dietary calcium do not appear to cause kidney stones and may actually protect against their development. [19,20] This is perhaps related

to the role of calcium in binding ingested oxalate in the gastrointestinal tract. As the amount of calcium intake decreases, the amount of oxalate available for absorption into the bloodstream increases; this oxalate is then excreted in greater amounts into the urine by the kidneys. In the urine, oxalate is a very strong promoter of calcium oxalate precipitation, about 15 times stronger than calcium. Other electrolytes Aside from calcium, other electrolytes appear to influence the formation of kidney stones.

Vitamin:

Despite a widely held belief in the medical community that ingestion of vitamin C supplements is associated with an increased incidence of kidney stones; the evidence for a causal relationship between vitamin C supplements and kidney stones is inconclusive. While excess dietary intake of vitamin C might increase the risk of calcium oxalate stone formation,in practice this is rarely encountered. The link between vitamin D intake and kidney stones is also tenuous. Excessive vitamin D supplementation may increase the risk of stone formation by increasing the intestinal absorption of calcium, but there is no evidence that correction of vitamin D deficiency increases the risk of stone formation.

kidney Stone Formation:

When CaOx concentration is 4 times above the normal solubility a crystal starts to form. If the CaOx concentration is 7 to 11 times higher than normal solubility the nucleation begins. In low urine volume, the presence of high calcium, high oxalate the supersaturation

(SS) of CaOx is increased Citrate in the urine forms soluble complex with urinary Ca. If urine has low citrate concentration SS CaOx is promoted to form CaOx stone. If urine pH is > 6.5, proportion of divalent and trivalent ions are increased then SS. The levels of urinary supersaturation of the different solutes determine the specific types of stones.

Stone Formation

Table:1 Relationship of Stone location to Symptoms

Stone Location	Common Symptoms
Kidney	Vague flank pain, hematuria
Proximal ureter	Renal colic, flank pain, upper abdominal pain
Middle section of ureter	Renal colic, anterior abdominal pain, flank pain
Distal ureter	Renal colic, dysuria, urinary frequency, anterior abdominal pain, flank pain

Management:

Appropriate management of symptomatic urolithiasis in patients depends on a few factors, specifically size, location and composition of calculi. The child's general health, comorbidities and complications, kidney function, anatomical variations of the urinary tract, andthe local availability of treatment and experience of physicians must all be children with

uncomplicated urolithiasis and small stones that are likely to pass spontaneously (< 4–5 mm) do not require urological intervention.

Conservative treatment includes adequate hydration and increased fluid intake, pain control and medical expulsive therapy to relax ureteric smooth muscle and facilitate stone passage Given the common underlying metabolic abnormalities and very high risk of kidney stone recurrence, children require a thorough metabolic evaluation and follow-up examinations. Change in diet, or long-term pharmacological treatment might be required. Interventional treatment of urolithiasis is generally advised in cases of severe obstruction and sur-decompression (e.g., acute renal failure, infection,obstructed solitary functioning kidney) or unsuccessful pharmacological therapy Indications and surgical techniques in patients are similar to those inadults, with the need for general a in children being the most important difference. Minimally invasive urological procedures are considered safe and effective;thus, open surgery should be limited to select children with large stones, congenital abnormalities, Extracorporeal shock wave lithotripsy is said to be the least invasive and safest interventional treatment method for proximal stones in children. In this procedure, shock waves are used to fragment the stones into small enough pieces to pass through the u stenting is rarely needed Extracorporeal shock wave lithotripsy is recommended for upper urinary tract stones of diameter ≤ 1.5–2 cm because its effective-ness is inversely proportional to stone size and decreases with lower calyx or ureteric calculi location.

Preventive Options for Urolithiasis:

Kidney stone can be avoided by addressing the cause of stone formation. The first episode of kidney stone formation or second- ary episodes, proper diet control and the use of suitable medicines. The underlying etiology and drug treatment for stone disorders, patients can take more water/liquid at least 2 litres per day. High sodium intake increases the risk of stone by reducing the reabsorption of renal tubular calcium and increasing urinary calcium. You may need to eat less meat, fish and poultry if you have very acidic urine and avoid vitamin D food. It is recommended to increase the intake of potassium-rich fruits and vegetables. Those who get calcium stones used to be advised to avoid dairy products and other calcium-rich foods because of invivo conversion of ascorbic acid to oxalate, vitamin C was involved instone formation. Therefore, it is recommended to reduce the intake of vitamin C.

Urine should be alkalinized to avoid calcium oxalate, cystine, and uric acid stones by eating a diet rich in fruits and vegetables, taking additional or prescription citrate, or drinking alkaline mineral waters. Gout needs to be controlled for uric acid stone form-ers, and sodium and protein intakes need to be limited for cystine stone formers. Urine should be acidified to remove calcium orthophosphate and struvite particles. For struvite rocks themost important step is to acidify the urine.

Conclusion

Incidence of urolithiasis is rising globally, despite notable advancements in the development of new medicines for urinary stone treatment. There are still many unknowns about the renal stone's genesis. However, it is evident that renal cell injury, crystal retention, apoptosis in cells, Randall's plaque, and related promoters or inhibitors of stone formation all play significant roles in kidney stone formation. Additionally, improving medication development may be aided by identifying novel therapeutic targets related to stone formation based on alterations in molecules and cells. Additionally, improving medication development may be aided by the identification of novel therapeutic targets related to stone formation that are based on molecular and cellular alterations. Therefore, a deeper comprehension of the urolithiasis pathways linked to stone inhibitors or promoters will be essential for developing drugs that dissolve stones.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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