



Kidney Stone Disease: A Primer

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ABSTRACT

Kidney stone disease is the aggregation of unwanted crystals usually within the kidneys. It is the most widespread disease of human urinary tract influencing about 12% of the universal population. Kidney stones are of various types, out of which the most prominent are the calcium oxalate stones. A lot of dietary factors & urinary risk factors are responsible for their formation. Most of the people suffer from kidney stones at various phases of their life. Moreover, the rate of occurrence of kidney stones is more prominent in males rather than in females. This review article discusses the types & symptoms of kidney stones, pathophysiological mechanism of their formation, risk factors, diagnosis, and possible treatment of renal stones.

Keywords: Kidney stones, risk factors, pathophysiology, diagnosis, management, treatment of kidney stones.

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INTRODUCTION

Human urinary system comprises of kidneys, ureters, urinary bladder & urethra. The kidneys are a pair of reddish-brown, bean shaped organs. Ureters are thin muscular tube which passes urine from the kidneys to the urinary bladder. The last part of urinary system is urethra which is a tube connected with the urinary bladder & its function is to pass out urine from the body. The elimination of nitrogenous waste from the body and the maintenance of homeostasis are the principal functions of the excretory system. The role of the urinary system is to filter impure blood, eliminate waste products from our body in form of urine. But, sometimes due to various dietary factors or some other risk factors, urine becomes excessively saturated with some substances which aggregate together into hardened crystals & result into the formation of kidney stones [1]. Kidney stones can develop anywhere in urinary tract. These are usually formed due to disturbance between the fluid and certain waste products in urine due to which concentration of stone-forming salts increases in the urine & stone formation will occur. Sometimes, kidney stones remain silent over months without causing any problem. Generally, the stones are very small in size & will excrete out through the urine. But, large stones cannot pass through the urine and requires a surgical treatment or some medications for their removal. These stones can cause extreme pain, blood in urine, burning sensation while urination or sometimes can even stop the passage of urine [2]. Kidney stones are the polycrystalline aggregates of various inorganic & organic matrix components [3]. Different types of chemical disturbances in the urine produce stones with diverse chemical constitution and different shapes. The most familiar urinary stones are calcium stones comprising of oxalate and phosphate. Other includes uric acid, cystine, struvite and drug-induced stones. Approximately 5% of the kidney stones are due to urinary tract infections & are known as struvite stones [4]. One percent of the kidney stones are cystine stones which are formed by over secretion of an amino acid cystine & are due to a genetic disorder. About 10 % of the kidney stones are uric acid stones that are formed as a result of waste product (uric acid) produced by the normal metabolism in our body. Generally, the uric acid dissolves in our blood & passes through the urine. But, sometimes when the body start producing excess of it, then our kidneys cannot eliminate it, resulting into the development of uric acid stones. Calcium stones are the most frequent type of kidney stones. Around 85% of the kidney stones are calcium stones in combination with oxalate and phosphate. About 1% of all stones are drug-induced stones [5]. These stones are formed due to intake of some lithogenic medicines viz. guaifenesin, triamterene, atazanavir, and sulfa medicines.

Symptoms of Kidney Stones – Various warning signs of kidney stones can be systemic, asymptomatic or there may be urinary tract symptoms like pain in renal portion or blood in urine (fig. 1). Some of the major warning signs of kidney stones are [6]:

- Sensation of pain in lumbar region of the body.

- Pain followed by nausea & vomiting.
- Cloudy or bad smelling urine.
- Blood in urine.
- Feeling pain during urination.
- Frequent urge of urination.
- Fever or chills.

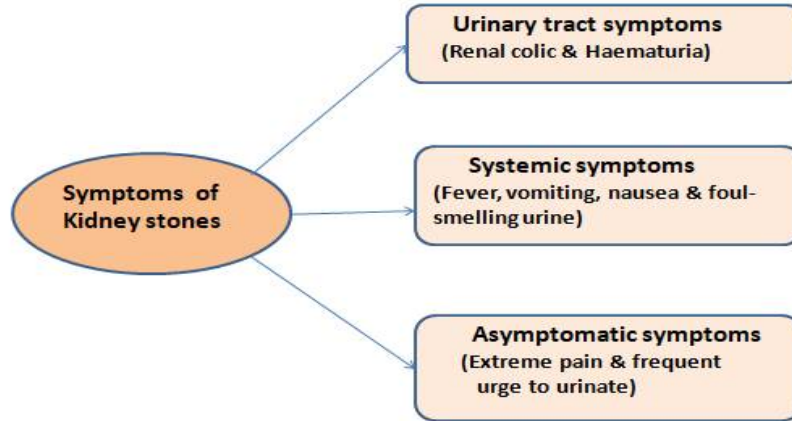


Fig 1. Symptoms of Kidney Stones

Risk factors for Kidney Stones:

The occurrence of renal stone disease has increased drastically in last 30 years. The kidney stone formation is a recurrent problem. Studies reveal that around 50 percent of the people who earlier had a kidney stone will develop it again within next 5 years. The recurrence rate without any precautionary treatment is roughly 10% in 1 year, 33% in 5 years & approximately 50% in next 10 years. The different risk factors related with renal stone disease are age, sex, climate, genetics, less fluid intake, diet, family history, & some medications (fig 2). High urinary calcium, high oxalate intake, high intake of animal protein, low urinary citrate, less urinary output, positive family history are the main risk factors for the formation of kidney stones. Besides this, persons working in hot & humid areas are more vulnerable to the kidney stone formation due to extreme sweating [7]. Moreover, probability of formation of kidney stones are more in men than women due to testosterone hormone in males as it increases the production of oxalate in the body.

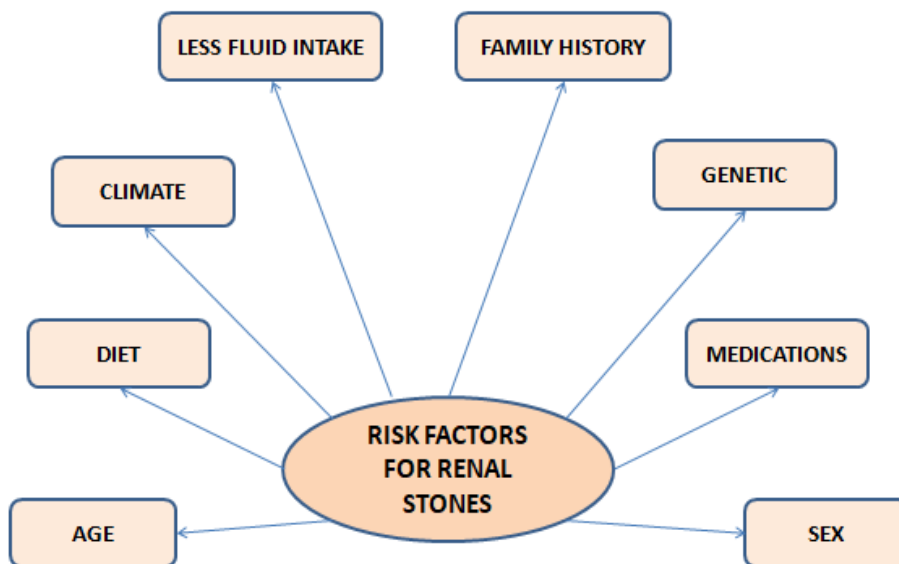


Fig 2. Risk Factors for Kidney Stones

PATHOPHYSIOLOGICAL MECHANISM OF KIDNEY STONE FORMATION

The process of stone formation involves numerous steps. First of all due to imbalance between various promoters & inhibitors, urine become overly saturated with certain microscopic substances and when the solubility product eventually reaches the formation product (Kf), then spontaneous homogeneous

nucleation will occur. Simultaneously, heterogenous nucleation will also occur due to renal cell injury that is caused by a number of risk factors, including hyperoxaluria, hypercalciuria, and hypocitraturia, & also due to cell debris, urinary casts and bacteria etc [8]. A decrease in urine flow, change in urinary pH, an increase in concentration of promoters & decrease in concentration of inhibitors are the four factors that lead to crystal formation [9]. If those crystals still remain in urine after urine excretion, it sticks to the renal epithelium, perhaps due to damage to the cell walls. Thus, crystal adhesion is necessary for the development of pathological stones. After the nucleation stage, the crystal growth starts. Crystal growth is a small lump of stone formed when crystals in urine stick together. Now, through the next process of crystal aggregation, small stones aggregate together to form a larger stone. After crystal aggregation, crystals are now retained and get accumulated in the kidney [10]. All these processes of stone formation are modulated by different types of inhibitor & promoters present in the urine [11]. The pathophysiological mechanism of formation of kidney stone is shown in fig.3

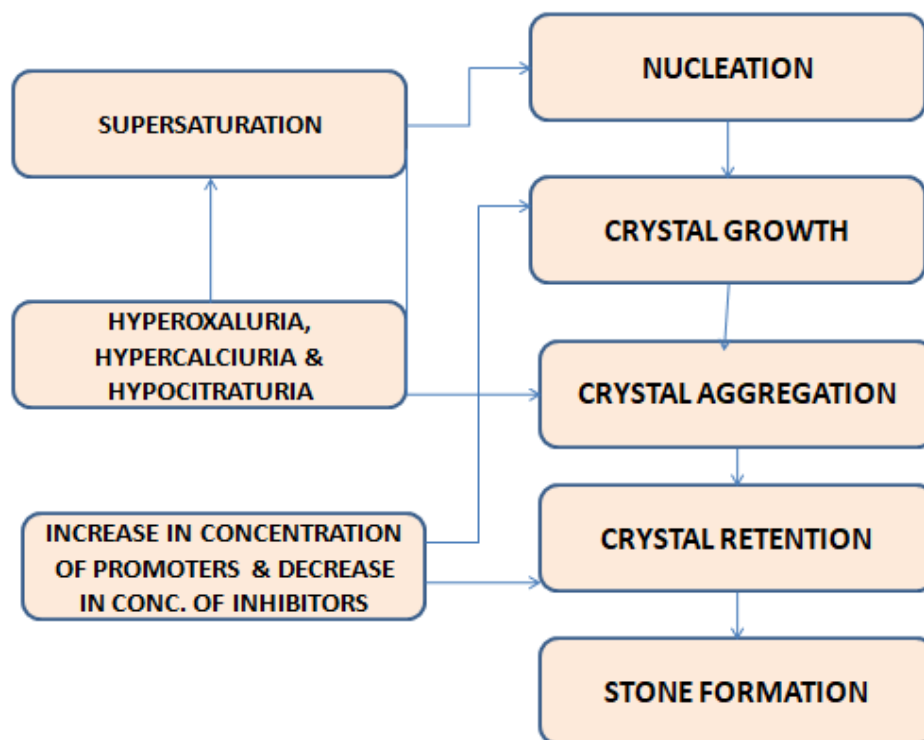


Fig 3. Pathophysiological Mechanism of formation of Kidney Stone

DIAGNOSIS OF KIDNEY STONES: Kidney stones can be diagnosed by various laboratory tests as well as some imaging techniques. Proper diagnoses of renal stone disease by blood & urine tests are essential to prevent stone formation.

Laboratory Evaluation for stones:

Blood Test - CBC (complete blood count) is done to find out the number for the presence of an increase in WBC count (Neutrophiles) and so on. Blood is screened for potassium, chloride, phosphate, bicarbonate calcium, uric acid etc

Urine Test - Microscopic study of urine shows presence of proteins, RBCs, pus cells, microorganism, cell casts and crystals etc. if any.

24-hour urine test – It is performed to measure daily urinary output, to detect concentration of various ions like magnesium, sodium, calcium, potassium, oxalate and phosphate, creatinine, urea, organic acids etc. This urine is also used to evaluate various physical properties of urine viz. SEC, pH etc.

Imaging Techniques for Evaluation of Stones:

Doctors use several imaging techniques for diagnosis of kidney stones like Magnetic resonance imaging (MRI), Ultrasound, KUB radiograph, computerized tomography (CT) scan, Intravenous pyelogram (IVP) etc [12].

TREATMENT: Kidney stones can be prevented by some dietary modifications based on the type of kidney stone [13]. Besides dietary modifications, some medications are also used to treat kidney stones (Table 1). Large stones can only be removed with the help of surgery [14].

Dietary recommendations/modifications:

Kidney stones can be prevented by making some modifications in their diet depending upon the nature of kidney stone, changes in intake of Na, animal protein, intake of Ca and oxalate, fiber- rich foods & fluid intake. Recommendations depending upon the nature of kidney stone are described in this section.

Calcium oxalate (CaOx) stones

Low urinary oxalate decreases the oversaturation of calcium oxalate in the urine. Hence the foods that are rich in oxalate content like spinach, rhubarb, and potatoes should be avoided. The absorption of oxalate is also associated with our calcium intake. The individuals with excessive urinary oxalate should be recommended to take sufficient calcium. Citrate, a byproduct of Krebs's cycle is a natural inhibitor of calcium oxalate (CaOx) and calcium phosphate (CaP) stones. Moreover, foods having high alkali content should be taken.

Calcium phosphate (CaP) stones

Higher concentrations of urinary Ca & lower concentrations of urinary citrate promote formation of CaP stones. Reduction of dietary phosphate is recommended so that phosphate excretion in urine is reduced.

Uric acid stones

Increasing urine pH is the prime cause for prevention of uric acid stone formation. This can be attained by increasing the intake of alkali rich foods & limiting the intake of acidic foods. Citrate or bicarbonate supplements are recommended so that urinary pH of around 6–7 is attained.

Struvite stones

These stones require surgical treatment for their removal. As these stones are formed due to urinary tract infection, so their recurrence can be avoided by the prevention of urinary tract infections.

Pharmacological treatment

For CaOx and CaP stones, thiazide and diuretics (with limited intake of sodium) may be given to decrease urine calcium [15]. In patients with low urinary citrate, alkali supplements like potassium citrate is given. Tiopronin, Penicillamine & Angiotensin converting enzyme inhibitor, is usually recommended for the treatment of cystine stones. Allopurinol & alkali treatment is recommended for uric acid stones & antibiotics are given to treat urinary tract infections.

Surgical treatment

Generally, stones which are less than 4 mm in diameter can pass spontaneously through the urine but the stones which are greater than 8 mm require surgical intervention & can only be removed by surgery. Nephrolithotomy is done by doctors to remove large stones inside the kidneys [16].

CONCLUSION

The increasing prevalence of kidney stones causes enormous economic burden on the society in terms of diagnosis and their treatment. The advancements in early diagnosis of kidney stones and treatment at earlier stage is the need of the hour. Since, kidney stones are also associated with a lot of other metabolic diseases viz. hypertension, diabetes, & obesity, thus various dietary modifications regarding occurrence and reoccurrence of kidney stones must be followed strictly. High intake of fluids, leaving sedentary lifestyle & implementing healthy lifestyle are some of the preventive measures for kidney stones.

Table 1. Pharmacological treatment for different Kidney Stones

S.N.	Type of Stones	Cause of stone formation	Pharmacological treatment
1	Calcium stones	Hypercalciuria	Hydrochlorthiazide Chlortalidone Indapamide
		Hyperoxaluria	Pyridoxine Alkali treatment
		Hyperuricosuria	Allopurinol Potassium citrate
		Hypocitraturia	Potassium citrate
2	Uric acid stones	Increasing urine pH	Allopurinol Alkali treatment
3	Cystine stones	Over secretion of the amino acid cystine	Tiopronin, Penicillamine Angiotensin converting enzyme inhibitor
4	Struvite Stones	Infection	Acetohydroxamic acid Antibiotics

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