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Review Article

UROLITHIASIS: OVERVIEW

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ABSTRACT
A 16-year-old boy died at E Amrah, Egypt, perhaps because he had a bladder stone, containing calcium phosphate and uric acid; what is remarkable is that this happened nearly 7000 years ago. Indeed, since trephining and circumcision had ritual a connotation, 'cutting for the stone' is probably the oldest purely surgical procedure. Even then, there was no lack of concepts concerning a etiology including overfeding, familial predisposition, and the composition of the blood. By 1663 Rofink had classified uroliths according to their size, shape, surface and colour and by the 18th century they were recognized to contain uric acid, oxalic acid, cystine and organic material. By the 19th century, phosphate stones were regarded as an affliction of poverty, urate stones as one of affluence. Even today 70% of humans with urolithiasis are obese, 90% of those with uric acid stones. Perhaps the strangest aspect of the history of urolithiasis is a relatively recent change in its epidemiology. Bladder stones were much more common than kidney stones until about 100 years ago, and especially common in children. This increase has been blamed on affluence and increased dietary protein but this seems hard to believe when poverty with high intake of vegetable protein was blamed for bladder stones and when an eightfold increase in calcium oxalate stones occurred between 1964 and 1971; during this period protein intake rose by less than 5%. Other factors such as low fibre and excess of refined carbohydrate associated with 'affluent' diets may predispose to urolithiasis. In particular, there may be peaks of increased urinary calcium following ingestion of sugary food or drinks.

KEY WORDS
Renal Damage, Urolithiasis, Calicium Oxalate

INTRODUCTION

Urolithiasis is derived from the Greek words ouron (urine) and lithos (stone). Urolithiasis refers to the accretion of hard, solid and non-metallic minerals in the urinary tract [1]. It is an ancient and common affliction whose clinical occurrence and presentation is described in Aphorisms of Hippocrates. Stone formation in the kidney is one of the oldest and most wide spread diseases known to man [2]. The formation of urinary tract stones is worldwide, sparing no geographical, cultural or racial groups. Recurrence rates are estimated at about 10% year, totaling 50% over a 5-10 year period and 75% over 20 years. Urolithiasis is quite common in developing and under developed countries [3], where the recurrence of endemic bladder stone is quite common due to the dietary proteins being mainly derived from plant sources. Urinary stone disease continues to

occupy an important place in everyday urological practice [4]. The average life time risk of stone formation has been reported in the range of 5-10 %. A predominance of men over women can be observed with an incidence peak between the fourth and fifth decade of life [5].

A kidney stone is a hard, crystalline mineral material formed within the kidney or urinary tract. Kidney stones are a common cause of blood in the urine and often severe pain in the abdomen, flank, or groin. Kidney stones are sometimes called renal calculi. The condition of having kidney stones is termed nephrolithiasis [6]. Urolithiasis is a complex process many remedies have been employed during the ages this stones are found in all parts of the urinary tract and kidney [7]. The present study is emphasized to explore the different stone formation, induced method of urolithiasis and medicament of urolithiasis. Epidemiological studies revealed that nephrolithiasis is more common in men (12%) than in women (6%) and is more prevalent between the ages of 20 to 40 in both sexes. Urinary calculi are much more likely to be found in individuals who have sedentary occupation. Blackcock reported that the incidence of urinary calculi was higher in administrative and sedentary personnel of the royal navy than in manual workers. [**Figures no 1**]

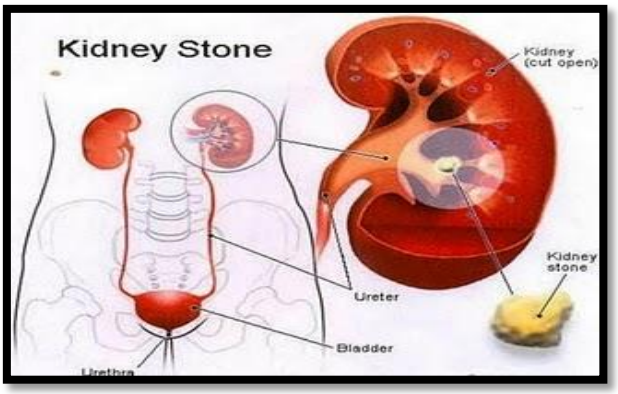


Fig 1: The incidence of urinary calculi was higher in administrative and sedentary personnel of the royal navy than in manual workers

ETIOLOGY

Stone formation is usually multi-factorial with more than one element increasing a patient‘s risk for stone formation [8]. The etiology of this disorder is multifactorial and is strongly related to dietary lifestyle habits or practices [9]. Increased rates of hypertension and obesity, which are linked to nephrolithiasis, also contribute to an increase in stone formation [10]. Stones are made up of multiple constituents but the first step in any stone formation is supersaturation of the urine. This results in crystallization of constituents and a nucleus for further stone growth and aggregation [11]. This step is usually inhibited by

compounds in our urine but in some patients these are absent or defective.

About 25% of patients with urolithiasis may be the result of a polygenic defect with partial penetrance. Several disorders that cause renal stones are hereditary and they are renal tubular Acidosis [12] and Cystinuria. Xanthinuria and dihydroxyadeniuria are rare hereditary disorders. A slightly higher rate of renal stone disease is reported in males than in females. Most of the urinary stone diseases were diagnosed at the fifth decade. The peak incidence of urinary calculi is from the twenties to the forties. Men are affected approximately 4 times more often than women. Recent evidence has shown an increase in pediatric cases [13]. The prevalence of urinary calculi is higher in mountainous, desert or tropical areas. Other high incidence areas are the British Isles, Scandinavian countries, Mediterranean countries, Northern India and Pakistan, Northern Australia, Central Europe, portions of the Malayan Peninsula and China. Incidence of urinary calculus disease in the United States is relatively high for its population [14].

Increased water intake and increased urinary output decrease the incidence of urinary calculi in those patients who are predisposed to the disease. The presence or absence of certain trace elements in water has been implicated in the formation of urinary calculi. For example, zinc is an inhibitor of calcium crystallization [15]. Dietary intake of various foods and fluids that result in greater urinary excretion of substances that produce stones has a significant effect on incidence of urinary calculi. Ingestion of excessive amounts of purines [16], oxalates, calcium, phosphate, sodium and other elements often results in excessive excretion of these components in urine. There is a relationship between occupation, social class and risk of stone formation. The risk of formation of urinary calculi was increased in the most affluent countries, regions, societies and individuals. These inhabitants have more disposable income to spend on animal protein, which leads to increased urinary concentrations of calcium, oxalate and uric acid [17].

Pathophyiology of Urolithiasis

Kidney stones are classified according to their chemical composition. Crystallization and subsequent lithogenesis can happen with many solutes in the urine [18]. For crystals to form, urine must be supersaturated with respect to the stone material, meaning that concentrations are higher than the thermodynamic solubility for that substance [19]. Calcium oxalate is the predominant component of most stones accounting for more than 80% of stones [20]. The remaining 20% are composed of struvite, cystine, uric acid, and other stones.

As mentioned above, the basis for calcium stone formation is supersaturation of the urine with stone-forming calcium salts [21]. [**Table no 1**]

Table 1: Major causes of calcium stone formation

Condition	Definition	Causes
Hypercalciuria	Urinary calcium excretion > 200 mg/d	**Absorptive hypercalciuria:** ↑GI calcium absorption renal. **hypercalciuria:** impaired renal Ca absorption resorptive **hypercalciuria:** Primary hyperparathyroidism.
Hyperoxaluria	Urinary oxalate excretion > 40mg/d	**Primary hyperoxaluria:** genetic Ox overproduction dietary **Hyperoxaluria:** excessive dietary intake **Enteric hyperoxaluria:** ↑GI oxalate absorption
Hypocitraturia	Urinary citrate excretion < 320 mg/d	**Distal renal tubular acidosis:** impaired renal tubular acid Excretion. **chronic diarrhea syndrome:** GI alkali loss **Thiazide-induced:** hypokalemia **Idiopathic hypocitraturia:** High animal protein diet, excessive physical exercise, high sodium intake.
Hyperuricosuria	Urinary acid excretion > 600 mg/d	Dietary urine excess, uric acid overproduction or over excretion
Hypomagnesuria	Urinary magnesium excretion < 50mg/d	Limited intake of magnesium-rich foods
Gouty diathesis	urinary pH < 5.5	Etiology unknown

Abbreviations: GI = gastrointestinal; Ca = calcium, Ox = oxalate; ↑= increased

CLINICAL SIGNS AND SYMPTOMS [22]

The clinical features of urinary tract stones are as follows:

- Urinary tract symptoms:

Pain- classic colicky loin to groin or renal, Haematuria- gross or microscopic, Dysuria and strangury

- Systemic symptoms:

Restless, writhing, Nausea, vomiting, Fever and chills Bloody, cloudly or foul-smelling urine

- Asymptomatic symptoms:

Incidental stones (one third may become symptomatic), Fluctuations in pain intensity, with periods of pain lasting 20 to 60 mints, Persistent urge to urinate[23].

Diagnosis [24]**:**

Clinical diagnosis is usually made on the basis of the location and severity of the pain. Pain in the back occurs when calculi produce an obstruction in the kidney. Imaging is used to confirm the diagnosis and a number of other tests can be undertaken to establish both the possible cause and consequences of the stone.

A number of diagnostic tests to diagnose kidney stones they are,

- Blood tests- full blood count for presence of a raised white cell count (Neutrophilia) etc.
- Urine test- Microscopic study of urine- show proteins, red blood cells, bacteria, cellular casts and crystals.
- Culture of a urine sample to exclude urine infection.
- 24-hour urine collection test.–measures total daily urinary volume, magnesium, sodium, uric acid, citrate, calcium, oxalate and phosphate.

Other diagnostic tests

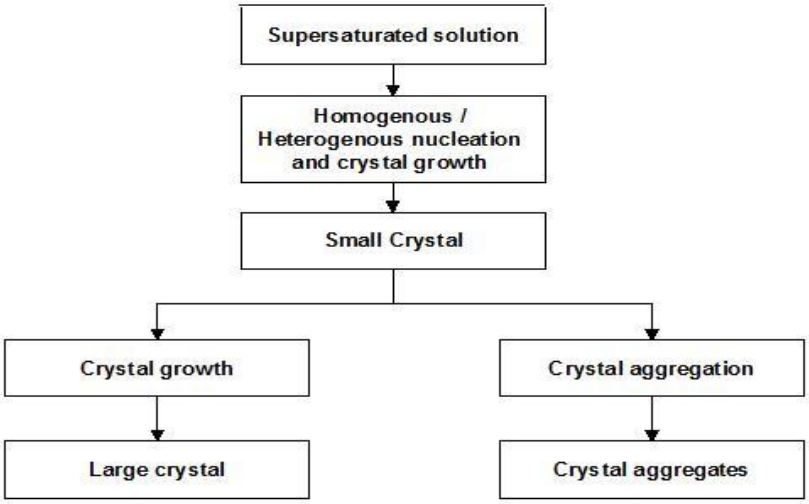
Kidney ureter bladder (KUB), X-ray kidney ultrasound, Intravenous pyelogram (IVP) and Computed Tomography (CT) scan [25].

PATHOGENESIS AND MECHANISM OF KIDNEY STONE FORMATION:

Renal stone formation requires that stone forming crystalloids in urine come out of solution. About 75% of all stones are calcium – based, consisting of calcium oxalate, calcium phosphate, and a mixture of oxalate and phosphate [26]. This Mixed stones have more than one component, such as a uric acid nidus in aggregation with calcium. Another 10% of renal stones are uric acid based, 1% cystine based, and the remainders are primarily struvite, in susceptible patients, stone formation, begins when urine super saturated with calcium, cystine, uric acid, struvite or oxalate. Calcium stone formation involves different phases of increasing accumulation of calcium oxalate (CaOx) and calcium phosphate (CaP). This process are promotes the stone formation,

- Nucleation,
- Crystal growth,
- Crystal aggregation
- Crystal retention.

Theories of stone formation



TYPES OF STONES AND INCIDENCE

The percentage composition of a urinary calculus contributes to the ability to predict the most probable cause of that calculus hence accurate quantitive analysis of calculus is critical in formulating a therapeutic plan that will be useful in preventing future stone disease in patients [27]. Urinary stones are about 97.5% crystalline aggregate and 2.5% organic matrix.[**Table no 2**]

Types of stones	Incidence
Pure calcium oxalate	33%
Mixed calcium oxalate and phosphate	34%
Struvite	15%
Uric acid	8
Pure calcium phosphate	6
Cystine	3
Artifacts and others	1

Table: 2 Types of Stones and Incidence

TREATMENT OF KIDNEY STONES

Management of any stone is dictated by stone location, composition, size and patient factors e.g. co-morbidities, solitary kidney and occupation. All management of stones can be thought of as acute, definitive and preventative. Preventative management involves education of patients to decrease their risk of stone disease by modifying diet and hydration. Hydration is the most vital step in prevention as chronic dehydration has been identified as a cause of urolithiasis. Increasing fluid intake has been shown to decrease stone incidence. Borghi et al showed

in calcium oxalate calculus formers that increasing the urine output to greater than 2 liters a day, results in a 12% recurrence in stone formation, compared to those with no specific fluid recommendations who had a 27% recurrence of calculi [28].

The goals of treatment are to control symptoms, render the patient stone free and prevent recurrence.

SURGICAL TREATMENT

Currently there are four methods of stone removal:

Extracorporeal Shockwave Lithotripsy (ESWL)

ESWL uses non-electrical shock waves that are created outside of the body to travel through the skin and body tissues until the shockwaves hit the dense stones. The stones become sand-like and are passed. For this procedure, patient's acre placed in a tub of warm, purified water or onto a water cushion machine that acts as a medium for transmitting these non-electrical shockwaves. There are several types of ESWL devices. In one device, the patient reclines in a water bath while the shock waves are transmitted. Other devices have a soft cushion on which the patient lies. ESWL is not ideal when stones are larger than 2 centimeters, about 0.8 inches.

[**Figures no 2**].

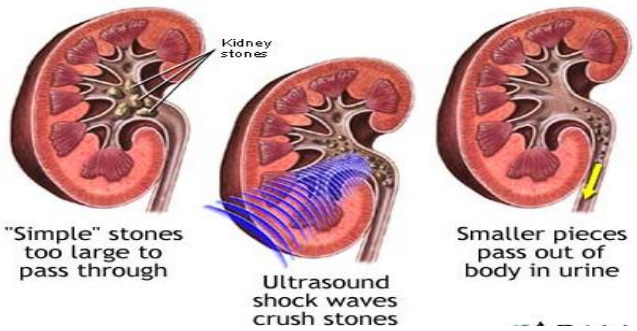


Fig: 2 Extracorporeal Shockwave Lithotripsy

Percutaneous Nephrolithotomy (PCNL)

Percutaneous nephrolithotomy, or PCNL, is a procedure for removing medium-sized or larger renal calculi (kidney stones) from the patient's urinary tract by means of a nephroscope passed into the kidney through a track created in the patient's back. PCNL was first performed in Sweden in 1973 as a less invasive alternative to open surgery on the kidneys. The term "percutaneous" means that the procedure is done through the skin. The purpose of PCNL is the removal of renal calculi in order to relieve pain, bleeding into or obstruction of the urinary tract, and/or

urinary tract infections resulting from blockages [29]. [**Figures no 3**]

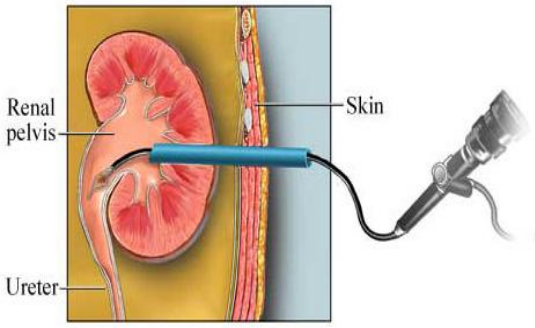


Fig: 3 Percutaneous Nephrolithotomy

Ureteroscopic Stone Removal

Ureteroscopic stone removal is achieved by passing a small fiber optic instrument (an ureteroscope) through the urethra and bladder into the ureter. The surgeon then locates the stone and either removes it with a cage-like device or shatters it with a special instrument that produces a form of shockwave. A small tube may be left in the ureter for several days after treatment to help the lining of the ureter to heal. [**Figures no 4**]

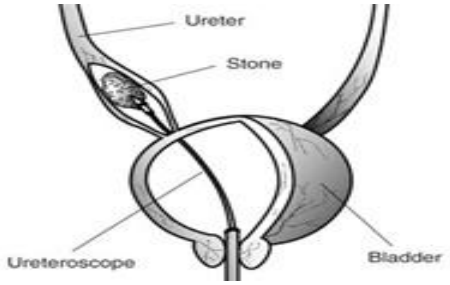


Fig: 4 Ureteroscopic Stone Removal

Open (incisional) Surgery

Open surgery involves opening the affected area and removing the stone(s). Another, less known procedure (called coagulum pyelolithotomy) also removes kidney stones. This procedure involves the injection of a liquid containing calcium chloride, cryoprecipitate, thrombin and indigo carmine into the kidney. This injection of substances forms a jelly like clot that traps the stones inside. Through an incision made in the kidney, the doctor extracts the stone with forceps.

Some stones are partially amenable to dissolution therapy; these include uric acid and cystine stones. Dissolution therapy is based on the solubility characteristics of the calculus in urine (pKa) and the manipulation of this such that more of the uric acid or cystine is soluble. Citrate based medications; such as potassium citrate; are used as dissolution therapy and can be used to

successfully manipulate the pH of the urine and pKa of the solutes with resultant dissolution of calculi. If implemented, the pH of the urine has to be monitored as if altered dramatically (increased to an alkaline state), this can cause the precipitation of calcium based stones. Ureteric stones greater than or equal to 5mm should be referred for a urological opinion15. They have a decreased likelihood of passing spontaneously and hence to prevent a long term sequelae should be managed surgically. Ureteric stones 4mm or less can be considered for medical expulsion therapy (MET). MET decreases the need for opioid analgesia, decreases the time to expulsion and decreases the need for surgery. Alpha blockers and Calcium channel blockers can both be used for MET. A trial of MET can be considered unsuccessful if the stone is still present at four weeks post commencement. If MET does fail, then the patient should be referred on for a urological opinion. As mentioned earlier staghorn calculi are associated with a high morbidity. All patients with stag-horn stones should be referred for urological input. Smaller renal stones that are symptomatic should also be referred for consideration of ureteroscopy or Extra Corporeal Shockwave Lithotripsy (ESWL). However asymptomatic smaller renal stones may be treated conservatively with observation. This does require ongoing imaging to ensure no growth of the stone. If the stone was to grow or cause symptoms then the patient should be referred for more definitive therapy [30].

Stone disease is a significant burden on the health care budget in a country like Samoa. Patient education, healthy lifestyle practice and prevention with early diagnosis will help in improving the health of the nation and reduce spending of the precious health dollar.

DISCUSSION

Urolithiasis is a complex process many remedies have been employed during the ages this stones are found in all parts of the urinary tract and kidney. The formation of such concretion encompasses several physicochemical events beginning with crystal nucleation, growth, aggregation, and ending by retention within urinary tract. The treatment of stone disease depends on the size and location of the stones. Stones larger than 5mm or stones that fail to pass through should be treated by some interventional procedures such as extracorporeal shock wave lithotripsy (ESWL), ureteroscopy (URS), or percutaneous nephrolithotomy (PNL).Natural history of residual stone fragments after ESWL shows growth and persistence of the calculus. In patients with residual fragments <5 mm or clinically in-significant residual fragments (CISF) with calcium oxalate and/or infection stones use of potassium citrate (6-8 gm in 2-3 divided

doses) has significantly ameliorated the outcome of these residual fragments by decreasing growth or agglomeration, allowing spontaneous passage and finally improving the clearance rate.

Potassium citrate is a better substitute than potassium bicarbonate because of more prolonged rise in urinary citrate and pH. The increment in urinary citrate is more pronounced with potassium citrate due to the renal excretion of small amount of absorbed citrate that has excaped oxidation. When compared with sodium citrate, potassium citrate reduces calcium excretion by augmenting the renal tubular absorption of calcium.Urinary sodium remains unaltered with potassium citrate but increases during sodium citrate therapy. In patients with hypokalemia, potassium citrate causes a more pronounced rise in citrate excretion than sodium citrate. The present study attempts to introduce the complex etiology of stone disease, highlight the natural history of stone disease left untreated and cover important points of contemporary management.

CONCLUSION

Urolithiasis is a common multifactorial disease that has been recognized and documented in medical literature since the Greek and Roman physicians. Urolithiasis encompasses both renal and ureteric stones. It is estimated to affect 102 per 100,000 per year New Zealanders, 15% of American men, 6% of American women and 3 -9% of Australians in their life-time. Stone disease varies with age, gender, ethnicity and season. Fifty percent of patients will have recurrent stone disease within 5 years, so it can be considered a disease for life. The medical management of urolithiasis is a rational approach based on the abnormal parameters detected on full investigation. However, in clinical practice it is very difficult as the patients may have all normal urinary parameters or multiple deranged parameters. In patients with all normal urinary parameters (idiopathic) the patient is advised dietary restriction and kept on periodic surveillance. In patients with multiple deranged parameters the drug approach in a permutation combination rationale is applied with periodic surveillance of the parameters at repeated intervals for dose modification or temporary discontinuation of the drug therapy. Both surgical and medical treatment is necessary for the complete management of patients of urolithiasis.

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