IOSR Journal Of Pharmacy *www.iosrphr.org*
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 8, Issue 2 Version. 1 (February 2018), PP. 30-42

Review on Uro-Lithiasis Pathophysiology and Aesculapian Discussion

Uthaya Chandirika Jayaraman [1] And Annadurai Gurusamy [2*]
Environmental Nanotechnology Division
Sri Paramakalyani Center for Environmental Sciences
Manonmaniam Sundaranar University, Alwarkurichi- 627 417, Tamilnadu, India.
Corresponding Author: Uthaya Chandirika Jayaraman

Abstract: Nephroliths are a common trouble worldwide with substantial morbidities and economic costs. This review describes focusing on update about the Pathogenesis formation of renal stone epidemiology. The most common adventure factors or aesculapian conditions associated with formation of renal stone, the current methods available for metabolic probe, dietary recommendations and medical treatment. Over the past 10 years, major progress has been made in the pathogenesis of renal stone. The incidence of nephrolithiasis (kidney stones) is rising worldwide, particularly in adult female and with rising age. Preventing recurrence is predominately specific to the character of stone (e.g., calcium oxalate, calcium phosphate, cystine, and struvite and uric acid stones); however, even when the stone cannot be retrieved, Managing diet, medication use, and food consumption can help prevent the organisation of kidney stones.

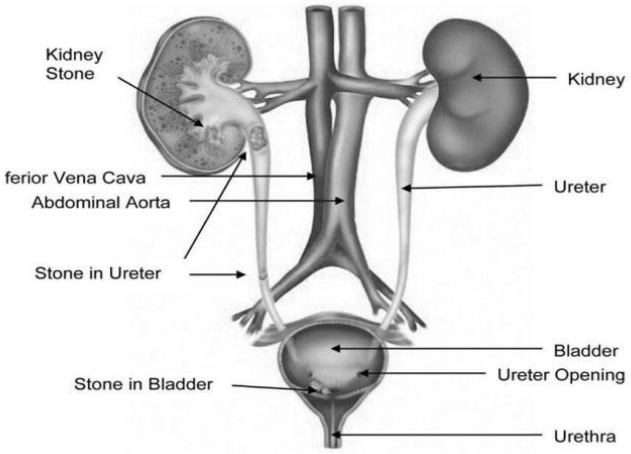
Keywords: Urolithiasis, Pathophysiology, Nucleation, Calcium oxalate, Treatments

---

Date of Submission: 09-02-2018 Date of acceptance: 24-02-2018

I. INTRODUCTION

Urolithiasis is a worldwide trouble afflicting human beings for diverse centuries. The yearly relative incidence of urolithiasis is about 10-15% in the western world, but can be as prominent in Middle East 20-25%. The incidence of urolithiasis alters in dissimilar countries. The recurrence rate without preventive treatment is approximately 10% at 1 year, 33% at 5 years, and 50% at 10 years. Various writers have attempted to research and advance process of stone formation in man (Doddametikurke et al., 2007). In India, more or less 5-7 million patients suffer from stone disease and leastwise 1/1000 of Indian universe necessarily hospitalization due to kidney stone disease. It is approximated that more than one million Australians probably have stones in their kidneys, although many will not be cognisant of this fact. These are mainly suffering from severe pain or because the stones are causing a block within the urinary tract ureteric obstruction and prevalent disorder of urinary system. The relative incidence of renal disorders particularly kidney stones have been raised in western nations in the final decades, in relation with economical growth (Ahmad-Reza and Soodabeh 2014).Nephroliths (called renal calculi from Latin ren, renes, "kidney" and calculi, "pebbles" in aesculapian parlance), which are also called nephrolithiasis or urolithiasis, educate when a accumulation of minerals or other materials form a minor stone in the kidney, ureter or bladder (Smith et al., 2010). Kidney acts as a barrier and filter for blood drosses. Dispatching waste products from the body and helping to regulate the chemicals levels. The kidneys play a role in controlling the acid-base balance in the body, regulating electrolyte balance as well as helping to control blood pressure. The urine drains from the kidney into the bladder through a narrow tube called the ureter. When the bladder fills and there is an urge to urinate, the bladder empties through the urethra, a much wider tube than the ureter (Zahid et al., 2009). The combination of these filtered substances and water is known as urine. Kidney stones (called renal calculi from Latin *ren, renes*, "kidney" and *calculi*, "pebbles" in medical parlance) are solid concretions or crystal aggregations formed in the kidneys from dietary minerals in the urine. The first evidence of urinary stones was found in an Egyptian mummy at E1 Amrah – Egypt 4800 B.C. Kidney stones are a relatively common problem. Kidney stone is termed as “Silent Disease" (Vyas Amit et al., 2012)



II. HUMAN URINARY SYSTEM AND KIDNEY FUNCTION

The two kidneys, parts of the urinary tract system, regulate the mineral composition, water content and acidity of the body (National Kidney and Urologic Diseases Information Clearinghouse (2009) *The kidneys and how they work*. Retrieved 2009 from http:// kidney.niddk.nih.gov/kudiseases/pubs/pdf/yourkidneys.pdf) Fig. 1. Shows the human urinary system they are also involved in the excretion of metabolic waste products and chemicals, are responsible for the production of certain hormones and vitamins, and also have a key role in blood pressure regulation. Removal of wastes occurs in tiny units inside the kidney known as nephrons; inside each nephron is a glomerulus which acts as a sieve-like filtering unit keeping proteins and cells in the bloodstream while allowing wastes to pass through. These wastes and any extra water become urine, which passes through tubes called the ureters into the bladder where it is stored until released during urination. Damage to the working units of the kidneys results in a reduction in the filtering capacity of one or both kidneys (National Kidney and Urologic Diseases Information Clearinghouse (2009) *The kidneys and how they work*. Retrieved 2009 from http:// kidney.niddk.nih.gov/kudiseases/pubs/pdf/yourkidneys.pdf)(Kidney Health Australia (2009) *Chronic kidney disease (CKD) management in general practice*. Melbourne, Vic: Kidney Health Australia)A critical function of the urinary system is the maintenance of normal composition and volume of body fluid, this is accomplished by glomerular filtration, tubular reabsorption, and tubular secretion of soluble and filterable plasma components, By such means, urine contains water, electrolytes, minerals, and hydrogen ions, end products of protein metabolism such as urea, uric acid, and creatinine. (Sasha Stumpers et al., 2013)

III. EPIDEMIOLOGY

A large number of people are suffering from urinary stone trouble all over the Earth. Not only the humans but animals and birds also suffer from the urinary stone trouble. Normally, three terms, i.e., incidence, prevalence, and lifetime prevalence, are frequently used in the epidemiological studies of urolithiasis. Once afflicted, urolithiasis tends to be recurrent in the most of cases (Moe et al., 2011). Recurrence rates after the first stone episode are 14%, 35%, and 52% at 1, 5, and 10 years, respectively. More or less 50% of patients with previous urinary calculi have a recurrence within 10 years (Sutherland et al., 1985). In a recent study, the recurrence rates are estimated at about 10% per year, totaling 50% over a 5-10 years period and 75% over 20 years (Moe 2006). The adventure of developing urinary calculi in adults appears to be more prominent in the western hemisphere than in the eastern hemisphere, although the highest risks of 20.1% have been described in Saudi Arabia. It has been reported that the incidence rates of urolithiasis are 5–9% in Europe, 12% in Canada, 13–15% in the USA (Ramello et al., 2000, Robertson and Hughes 1994). The incidence rate increases to 20-25% in the Middle East, because of increased risk of dehydration in hot climates (Potts 2004). According to the data of a nationwide survey on urolithiasis in Japan between 1965 through 1987, 5.4% of the universe may be expected to develop a urinary calculus at least once in their life time (Yoshida and Okada 1990). The occurrence in some areas is so alarming that they are known as 'Stone Belts'. The areas of high incidence of urinary calculi include British islands, Scandinavian countries, Central Europe, Northern Australia, Mediterranean countries. The Afro-Asian stone forming belt stretches from Sudan, Egypt, Saudi Arabia, United Arab Emirates, Iran, Pakistan, India, Myanmar, Thailand, and Indonesia to the Philippines in these areas of the world, the disease affects all age groups (from less than 1 year old to more than 70 years old) with a male-to-female ratio of 2:1

(López, and Hoppe 2010). Studies conducted over the last half century, suggest that the incidence has been steadily increasing (Hesse et al., 2003, Stamatelou., et al 2003). In the last 10 years, the diagnosis of urolithiasis was increased approximately by a 50% (Roehrborn C and McConnell 2007). In Germany there are approximately 7, 50,000 cases of renal stone per year (Strohmaier 2000). Recent reports propose a continuing upward trend in stone rates in Germany. In India, the "stones belt" concerns parts of Gujarat, Rajasthan, Maharashtra, Punjab, Haryana, Delhi and states of north-east (Singh et al., 1977, Colabawalla 1971, Singh et al., 1978, Pendse et al., 1984, Singh et al., 1988, Hussain and Billimoria 1990). The Saurashtra and Kutchchh region of Gujarat has higher prevalence of urinary stones (Srivastava and Alon 2005, Ding 2009).Although renal stone is perceived as an acute illness, there has been growing evidence that renal stone is a systemic disorder that leads to end-stage renal disease (Worcester et al., 2014). The prevalence of this disease has been increasing among males and females of all ages, indicating a potential environmental cause in add-on to genetic predisposition (Yoshida et al., 1999).

3.1 Body size and mass

The tie between calcium intake and renal stone formation varies with body size (Taylor et al., 2004). Larger body size may result in increased urinary excretion of calcium, oxalate and uric acid, thereby increasing the risk for calcium-containing kidney stones. Obesity and weight gain leads to risk of kidney stone formation may be more in women than in men (Taylor et al., 2005).

3.2 Economics

The health prices affiliated with treatment of stone disease has risen over recent years. These have been estimated in the USA at $ 2-5.3 billion per year and about € 54.38 million in Germany (Strohmaier and Hormann 2000, Chandoke 2002, Porena et al., 2007). Moreover, it has also been accounted in the UK, that all stone episode prices the local health assurance almost £2000 (Robertson 2003). Non with standing that the prevalence and relative incidence of renal lithiasis are approximated at 5-10% per year separately, and that the recidivates occur in 50-70% of all cases (Saita et al., 2007). The arising aesculapian price of treatment of stone disease, is another stark reminder that prevention of stone formation is of great importance.

3.3 Age and Sex

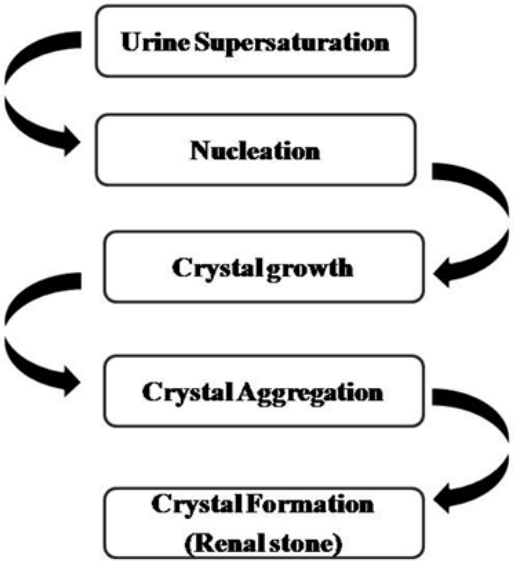
The disease affected all age groups from less than 1 year old to more than 70 year old peoples, with a male and female ratio is 2:1. The incidence of formation first kidney stone between the ages of thirty and seventy vary between approximately 100-300 per year in men and 50-100 per women i.e. 6%–9% in males and 3% – 4% in females (Johnson et al., 1979, Hiatt et al., 1982, Soucie et al., 1994, Curhan et al., 1997, Madore et al., 1998, Sowers et al., 1998, Nabi et al 2007 , Stamatelou et al., 2003, Baker et al., 1993). The development of calcium oxalate stones was formed in between 50-60 years old. However the increased incidence of recurrence in patients, that the older age may be attributed to the influence of ageing and diet. The relation between diet and kidney stones may be different in different age group. The intestinal absorption of many nutrients that influence stone formation, such as calcium, may be reduced in the elderly (Saltzman et al., 1998, Abrams 2001). In men, the incidence of kidney stones declines markedly after 60 years old (Hiatt et al., 1982, Curhan et al., 1993, Souice et al., 1994), suggesting that the pathophysiology of nephrolithiasis is different in the elderly. Older stone formers excreted less urinary calcium than their younger counterparts (Goldfarb et al., 1994) and may exhibit defects in urinary inhibitors of crystallization (Bergland et al., 2002). Increased incidence in males also has been attributed to increased dietary protein intake, which increases urinary excretion of phosphates, magnesium and reduces urinary citrate concentration. The lower risk of stone formation in women was attributed initially to increased urinary citrate concentrations due to the lower urinary saturation of stone forming salts (Welshman et al., 1975), while later reports indicated that endogenous estrogen and estrogen treatment in postmenopausal women may reduce formation stone recurrence by lowering urinary calcium and calcium oxalate saturation. Estrogen may also help to prevent the formation of calcium stones by keeping urine alkaline and raising protective citrate levels (Heller et al., 2002). Experiments in animals demonstrated that testosterone promoted crystal growth by suppressing osteopontin expression in the kidney and increasing urinary oxalate excretion while estrogen possibly inhibited stone formation by increasing osteopontin expression in the kidney and decreasing urinary oxalate excretion (Yagisawa et al., 2001, Parmar 2004).

IV. PATHOGENESIS OF RENAL STONE FORMATION

The physical process of stone formation is a complex cascade of events, result from the growth of crystals leads to stones formation (Kok 2002). The process of stone formation is depend on volume of urine, comprise concentrations of calcium, phosphate, oxalate and sodium ions (Mandel 1989). High ion levels, low urinary volume, low pH, and low citrate levels privilege the formation of urinary calculi. The pathogenesis of urinary calculi formation is the end result of the fundamental multi-step physicochemical processes Fig.2.The

genetic, metabolic, environmental and dietetic factors are involved in the pathogenesis of urolithiasis, all of them privilege the crystallization of salts, formed in inside renal tubules. Crystalluria is often observed in normal individual, but if crystals remain apart from each other. They are washed away by urine flow; however, some chemical and electrical forces trigger the process of aggregation. The crystals aggregate and attaches to epithelium, which allows them to growing and forming the stones (Khaskhali et al., 2009).

Fig 2 Pathogenesis of renal stone formation



The kidney stone formation in the three broad conceptual categories requires:

- Excessive concentration of solutes in excess of their solubility in the urine.
- Imbalance of modifiers (promoters and inhibitors) and crystallization in the urine.
- Epithelial abnormalities that allow attachment and subsequent growth of these crystals in to stone
- Above the factors act in concert and eventuating in the formation of the kidney stones (Moe et al., 2010).

Moreover, calcium oxalate (Caox) crystals, the main constituent of human urinary calculi may adhere in the plasma membrane of epithelial cells by a specific manner and followed by endocytosis of the crystals resulting to cell damage or death. Damaged cells exhibit a proliferation response and increase the fibrogentic synthesis, it substance promoting additional stimulus for crystal growth (Mirian et al., 2010). Calcium stone formation involves different phase of increasing accumulation of Caox and cap-nucleation, crystal growth, crystal aggregation and crystal retention (Lingenman 1986).The physico-chemical analysis describes stone formation as a supersaturated solution in which homogenous or heterogeneous nucleation can lead to initiation of crystal formation, which can then aggregate and growth (Bhuskute et al., 2009).

4.1 Nucleation

Nucleation is the formation of a solid crystal phase in a solution. The stone formation starts from the nuclei, which means the process of new crystal formation. It is an essential step in renal stone formation the term super saturation refers to a solution that contains more of the dissolved material than could be dissolved by the solvent under normal circumstances. Crystal nucleation is the first step in the formation of stone which can either be homogeneous nucleation of a salt occurs in unstable zone of super saturation. Crystalluria and stone formation seem to be the result of hetrogeneous nucleation induced by promoters. Promoters probably present preformed surfaces that reduce the surface energy required for crystallisation. During crystal growth, the free energy of solution continues to decrease as new crystal components are taken from the solution and become part of the crystal structure. Once formed, the crystalline particles can bind to each other in either an oriented or random growth pattern and then grow into a larger particle (Nirlep Chhiber et al., 2014).

4.2 Crystal growth

After the nucleation process, the micro crystals can mature by epitaxially mediated crystal growth. Epitaxy is oriented overgrowth of one crystalline material on to a substrate crystalline lattice. Monoepitaxial growth refers to the adsorption of the molecules or ions one by one on the crystal surface from supersaturated urine and heteroepitaxial growth refers to direct growth of one crystal on a surface of different composition and

the surfaces of crystal and substrate (Nirlep Chhiber et al., 2014). Several atoms or molecules in a super-saturated liquid start forming clusters. The total free energy of the cluster is increased by the surface energy; however, this is significant only when the cluster is small. Crystal growth is determined by the molecular size and shape of the molecule, the physical properties of the material, pH, and defects that may form in the crystal's structure. Crystal growth is one of the prerequisites for particle formation. (Qiu et al., 2004)

4.3 Aggregation

Aggregation is a process in which crystal nuclei bind to each other to form larger particles. The initial nuclei can grow by further addition of desired salts. A small inter-particle distance increases the attractive force and privileges particle aggregation. Crystal aggregation plays an important role in stone formation. In various steps of stone formation, crystal aggregation is a more significant step and then nucleation and growth. Aggregation of particle in solution is determined by a balance of forces, between aggregating effects and disaggregation effects and also a small inter particle distance that privileges particle aggregation (Basavaraj et al., 2007).

4.4 Retention

Crystal retention can be caused by the association of crystals with the epithelial cells lining. Urolithiasis requires formation of crystals followed by their retention and accumulation in the kidney. Another process that may lead to stone formation is crystal retention. i.e., crystal precipitation, growth, and aggregation, which results in urinary stone formation, if the nucleated crystals were flushed out by urinary flow. Retention might also depend on the composition of the renal tubular epithelial cell surface (Verkoelon et al., 2000).

V. URINARY RISK FACTORS

Urolithiasis is associated with a variety of abnormalities in urinary composition, which are due to dietary indiscretions, physiological-metabolic disturbances or both (Pak 2004a, Taylor and Curhan 2004). These urinary risk factors have been identified as those urinary characteristics that are widely accepted to influence the likelihood of calcium stone formation or recurrence and routinely measured as part of the metabolic investigations of both calcium stone formers and non-stone formers (Rodgers 2002, Sutton 2006). A number of risk models of stone formation have been developed over the years (Robertson et al. 1978, Khan 1997, Robertson 2003, Jaeger and Robertson 2004). Fortunately, the correction of abnormal risk factors by dietary modification and pharmacologic intervention has been shown in several studies to reduce the risk of stone formation as well as prevent recurrent stone formation (Massey et al., 1993, Anbazhagan et al., 1999, Baggio et al., 2002, Rodgers and Lewandowski 2002, Massey 2003, Jaeger and Robertson 2004, Pak 2004b, Taylor and Curhan 2004, Goldfarb et al., 2005, Siener and Hesse 2005, Taylor et al., 2005, Hesse and Straub 2006, Thomas et al., 2008).

5.1 Stone types Stone size and Location

Urinary stones are typically classified by their location in the kidney (nephrolithiasis), ureter (ureterolithiasis) or bladder (cystolithiasis), or by their chemical composition (calcium-containing, struvite, uric acid, or other compounds) (Potts 2004). Table 1. The size of a stone is usually given in millimetres (mm), using one or two-dimensional measures. Stones can be stratified further into those measuring up to 5 mm, > 5-10 mm, > 10-20 mm, and > 20 mm. A stone can be classified according to its anatomical position in the urinary collecting system at diagnosis: upper calyx, middle calyx or lower calyx, renal pelvis, upper ureter, middle ureter or distal ureter, and urinary bladder.

Name of stone	Approximate incidence	Constituents
Calcium oxalate	70 % of all stones	Calcium, oxalate
Calcium phosphate	10 % of all stones	Calcium, phosphate
Uric acid	5-10 % of all stones	Uric acid
Struvite	10 % of all stones	Calcium, ammonia, phosphate
Cystine	Less than 1% of all stones	Cystine
Medication-induced stones	Less than 1% of all stones	Composition depends on medication or herbal product (examples include indinavir, ephedrine, guaifenesin, silica)

Table 1 Types of kidney stone

5.2 Calcium stones

The calcium oxalate stone occupies a lion's share of the space. These calcium crystals are formed through the combining of calcium and oxalic acid. Calcium is simply an abundant urine atom. Oxalic acid is a dead end waste product from the kidneys. Aside from primary and enteric hyperoxaluria, most cases found in patients have`mild hyperoxaluria', defined by levels of urinary oxalate from 40-100 mg per day with a reported frequency is 12-63 % (Borsatti 1991)The kidneys themselves are not obviously injured except when obstruction lasts too long, or something happens during surgery. The calcium oxalate stones come in two varieties, monohydrate and dehydrate, the former are harder and therefore more resistant to fragmentation by lithotripsy. Likewise, the former appear more often when elevated levels of urine oxalate are present.

5.3 Calcium phosphate Stones

An increase in urinary phosphate causes an increase in calcium phosphate complexation thereby reducing the risk of calcium oxalate crystallization (Schwille et al., 1989, Baumann et al., 2001). Calcium phosphate occurs in stones as either apatite (the principal constituent of bones and teeth) or brushite (calcium monohydrogen phosphate). Evan et al., 2005 reported that the calcium phosphate presenting as a constituent of kidney stones in amounts ranging from 1-10 % (Evan et al., 2005). Although, calcium phosphate stones have more numerous and often larger stones, Brushite stones are very hard and do not break well with shock wave treatments. Hydroxyapatite crystals can plug the kidney tubules and injure kidney cells. For these reasons, prevention may be more urgent than for calcium oxalate stones (Mandel and Mandel, 1989, Coe et al., 2005).

5.4 Uric Acid Stones.

Uric acid stone may consist of uric acid only or containing calcium. Uric acid is a byproduct of ingested or endogenous purine metabolism and is excreted in the urine primarily in insoluble form (Moe et al., 2002; Bahuguna et al., 2009) It is the same crystal that causes gout in an arthritic condition. The solubility of uric acid depends on the acidity or alkalinity of the urine. In acid urine, pH less than 5.5, uric acid crystals precipitate leading to stone formation. If urine is alkaline, uric acid remains soluble and doesn't precipitate out. The stones can be red or orange because uric acid crystals absorb hemoglobin breakdown products that are red orange pigments in urine. Sometimes uric acid crystals pass in urine as a red orange gravel.Uric acid stones become very large, even enough to fill up the entire collecting system of the kidney. Because of uric acid does not connect itself to some other atom or molecule to make a crystal. In the way that calcium must bond with oxalate or phosphate ions to make crystals of calcium oxalate or calcium phosphate stones. Crystals of uric acid can form very fast in seconds and pass as orange gravel in the urine. The whole process depends almost completely on the acidity of the urine (Nikhil et al., 2010).

5.5 Struvite stones

Struvite stones which are often branched ('staghorn" stones) occur more often in women's and in patients who have chronic urinary obstruction or a neurologic disorder. Struvite stones are usually radio opaque on standard radiographic imaging but patient with struvite calculi may experience flank pain and have signs of systemic infection. These stones are also call triple phosphate, struvite or infection stones. These stones develop when the urine pH is higher than 7.2 and ammonia is present in the urine. Bacteria that produce urease act on the urea present in urine to form ammonia. The most common bacteria associated with struvite stones is *proteus*, but other bacteria such as *Staphylococcal aureus, Klebsiella pneumoniae* and *Pseudamonas putida* may also be implicated. Struvite stones occur more often in females than males with a ratio of 2:1. Urine is filled with urea, and if the soil bacteria get into the urinary tract they break it down to ammonia. The ammonia makes the urine around the bacteria extremely alkaline, and the ammonia crystallizes with magnesium and phosphate that are always in urine to make struvite. Treatment is a mix of thoughtful and skilled surgery and selection of antibiotics after such surgery to kill bacteria that remain. If the stones are a mixture of struvite and calcium crystals, new calcium stones need to be prevented. There is good evidence that failure to treat struvite stones can lead to an increased risk of renal loss, sepsis and death (Phillip and Hall, 2009).

5.6 Cystine stones

Lemon yellow with a sugary coating these form only in people who have an inherited kidney disorder called cystinuria. The kidneys function well except that they permit abnormal amounts of four amino acids to enter the urine. The process is fast, and in people who lose the amino acid in their urine because of cystinuria the amount of material available to make stones is large, so stone growth can be rapid. Cystinuria is an autosomal recessive disorder that causes impaired renal tubular reabsorption of cystine, ornithine, lysine and arginine. This leads to increased urinary excretion of these compounds, but the only one that forms stones are the cystine like uric acid and struvite. Like phosphate stones their crystals often block kidney tubules and can damage their cells. Stones may begin in childhood. Treatment is very effective but almost always requires very large amounts

of fluids to dilute the urine. The few drugs that help prevent them have side effects so fluids are always the foundation of treatment.

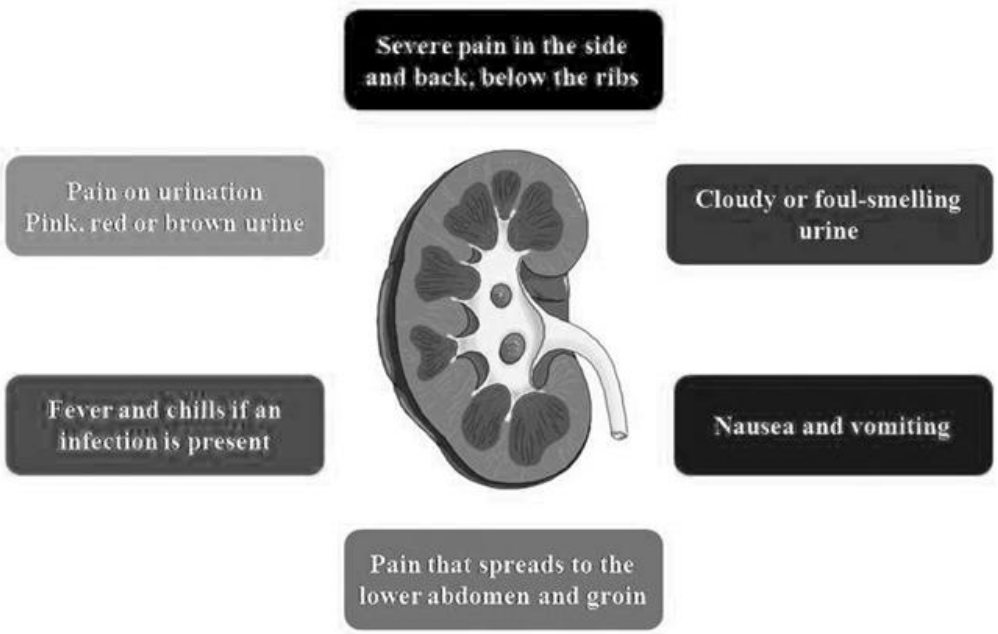
5.7 Pain from Stones

Passage of a kidney stone or renal calculus is often rated as one of the top two pains in humans, which are childbirth and passage of a kidney stone. Women routinely compare passage to labor pains. They often report that labor pains are less intense. The pain is caused by urinary obstruction, not the existence of the stone in the kidney.

VI. SYMPTOMS OF KIDNEY STONES

Symptoms of stone passage include "flank pain" Fig 3. The flank is the region of your body on your back protected by the last two ribs. There may be radiation of the pain around to the lower abdomen on the affected side. Patients frequently experience nausea and occasionally vomiting. As the stone passes out of the kidney into the upper ureter, men may experience testicular pain and women may have a similar pain in the vagina or groin area. If the stone is very low in the ureter but near the bladder, then there will likely be an onset of frequent urination that can be mistaken for a urinary infection. Bladder infection, cystitis, and urinary tract infection are alternate terms for urinary infections.

Fig 3 Symptoms of Kidney Stones



6.1 Dietary role in lithiasis

Modern lifestyle, dietary habits and obesity emerge to be the promoters of idiopathic stone disease. Modern diets containing a lot of animal protein, refined carbohydrates and salts act on the metabolism like an acid concentration. To overcome this disadvantage, a sufficient supply of potassium and alkali is required. It is important to know that calcium should not be restricted. Usually the body does not absorb more calcium, certain conditions, can be absorbed leading to excessive passage in the kidneys (Borghi et al., 2002).Recent studies report that actual protein consumption in children in Europe and North America are 3-5 times higher than recommended (Prentice et al., 2006). The decreased urinary pH may potentiate uric acid lithiasis, it enhance citrate reabsorption in the proximal tubules, thus decreasing the excretion of this important inhibitor of crystallization (Trinchieri et al., 2006).A nutritionally poor diet that is low in animal protein and calcium, which is the main factor that leads to the development of bladder stones in children in undeveloped countries. This leads to the formation of urine with a relatively high content of ammonium and urate ions and consequently to the formation of ammonium acid urate stones (Rizvi et al., 2002). Recent studies have suggested an increased prevalence of urolithiasis and recurrence associated with obesity with elevated urinary excretion of calcium, sodium, uric acid and oxalate (Lee, 2008).

6.2 Medical management of kidney stones

There are a number of practices for treatment of urinary calculi, including surgery, and endoscopic procedures such as ureterscopy percutaneous nephlithotomy and extracorporeal shock wave lithotripsy. Medical management of urolithiasis is still a challenge for modern medical practice (Mohanty et al., 2010, Nabi et al., 2007, Seitz et al., 2009). Doctors can usually diagnose kidney stones by asking about symptoms and examining patient. Further tests may be done to confirm the diagnosis and to reveal the size, location and type of stone (Cox and Coupland, 2010).

Blood tests

These are done to identify excess amounts of certain chemicals related to the formation of stones and to check the presence of infection by blood cell counts.

Urine analysis

It helps to look for signs of infection and estimation of values of various contributing factors viz. oxalates, calcium, cystine, citrates, magnesium, phosphates, etc.

Taking an X-ray image

Stones that contain calcium are usually seen as white spots on X-ray images (Miller et al., 2007).

An intravenous urogram (IVU)

This involves an injection of a special dye that shows up the whole urinary system on X-ray images, revealing stones that can't usually be seen. Traditional intravenous pyelography is no longer the primary method of investigation in patients with renal colic (Shokeir, 2002),

Abdominal Ultrasonography

Abdominal ultrasonography has limited use in the diagnosis and management of urolithiasis. Although ultrasonography is readily available, quickly performed and sensitive to renal calculi, it is virtually blind to ureteral stones (sensitivity: 19 percent), which are far more likely to be symptomatic than renal calculi (Yilmaz et al., 1998).

6.3 Plain Film Radiography

Less radiopaque calculi, such as pure uric acid stones and stones composed mainly of cystine or magnesium ammonium phosphate, may be difficult, if not impossible, to detect on plain-film radiographs. Although 90 percent of urinary calculi have historically been considered to be radiopaque, the sensitivity and specificity of KUB radiography alone remain poor (sensitivity: 45 to 59 percent; specificity: 71 to 77 percent) (Levine et al., 1997).

6.4 Non-contrast helical computerized tomography

It produces pictures from a series of X-ray images taken at different angles - it is sometimes used to diagnose kidney stones and is thought to be the most accurate diagnostic test. It has become the first-line investigation in a number of centers (Masarani et al., 2007). This imaging modality is fast and accurate and it readily identifies all stone types in all locations. Its sensitivity (95 to 100 percent) and specificity (94 to 96 percent) suggest that it may definitively exclude stones in patients with abdominal pain (Chen et al., 1999; Vieweg et al., 1998; Dalrymple et al., 1998; Boulay et al., 1999).

6.5 Shock wave lithotripsy

Shock wave lithotripsy is an external source to the patient that propagates through the body before being focused on kidney stone waves that cause stone fragmentation directly by producing mechanical stresses or indirectly by the collapse of cavitation bubbles. This is the most common treatment for urolithiasis, which can have slightly side effects (Evan et al., 2005).

6.6 Extracorporeal Shockwave Lithotripsy (ESWL)

ESWL is a non-invasive procedure which uses shock waves to fragment calculi. This proficiency is the most widely used method for dealing renal and ureteral stones. However, intervention success rates depend on stone composition, size, properties and location of the stone as well as the orchestration type and frequency of shock (Knoll, 2007, Tombolini et al., 2010, Coe, 2005). Some oral medicinal drug have positive effects, they are not effective in all patients, but citrate is one of the majority widely used medical therapies for preventing urinary stone disease (Serhat and Kupeli, 2006, Mattle and Hess, 2005). The medical treatment of urolithiasis is aimed at assisting the patient from further growth of existing stones and development of new stones, thus decreasing morbidity and the need for surgical intervention hence, under these circumstances medical treatment (Mohanty et al., 2010).

VII.PREVENTION

Despite the major expert achievements for stone removal in the last three decades the problem of recurrence rate of kidney stones is about 15% in the first year and as high as 50% within five years of the initial stone. Efficient kidney stone prevention is depending on the stone type and the identification of risk factors for stone formation. An individualized treatment plan incorporating dietary changes supplements and medications can be developed to help prevent that formation of new stones. Stone disease patient should be instructed to increase the fluid intake in order to maintain urine output of at least 2 L/D (Alon et al., 2004).

VIII. CONCLUSION

The present reassessment conveys entropy about the pathophysiology of kidney stone stone, types and treatments of urolithiasis. Kidney stone disease remains a major public health burden. Its pathophysiologic mechanisms are complex, majorly because it is polygenic disorder Dietary agents play a essential part in urinary calculus formation, and dietary alteration can reduce the risk of stone recurrence. Treatment is successful if attended in early stage itself. Surgical treatment is more effective. Stone disease is a significant burden on the health care budget in a country. Patient education, healthy lifestyle practice and prevention with early diagnosis will aid in improving the health of the nation and reduce spending of the precious health dollar.

ACKNOWLEDGMENT

Authors gratefully acknowledge the DST-FIST-sponsored program of the Department of Science Technology, New Delhi, India for funding the research development (Ref. no. S/FST/ESI-101/2010) and in carrying out of this work.

REFERENCES

[1]. Abrams SA (2001), Calcium turnover and nutrition through the life cycle, Proc Nutr Soc 60: 283–289.
[2]. Ahmad-Reza Gohari, Soodabeh Saeidnia (2014) the role of herbal medicines in treatment of urinary tract diseases, J Nephropharmacol; 3(1): 13–14.
[3]. Alon, U., Zimmerman, H., Alon, M., (2004) "Evaluation and treatment of pediatric idiopathic urolithiasisrevisited," Pediatr Nephrol., Vol.19 (5), pp.516-20.
[4]. Anbazhagan M, Hariprasad C, Samudram P, et al. (1999) Effect of oral supplementation of vitamin E on urinary risk factors in patients with hyperoxaluria. J Glin Biochem Nutr; 27: 37-7.
[5]. Baggio B, Budakovic A, Priante G, et al (2002) Dietary fatty acid supplementation modulates the urinary excretion of calcium and oxalate in the rat Insight into calcium lithogenesis. Nephron; 91 (93): 486-1.
[6]. Baker PW, Coyle P, and Bais R, Rofe AM (1993) Influence of season, age and sex on renal stone formation in South Australia. Med J Aust 159:390–392.
[7]. Basavaraj, Chandra Shekhar Biyani,Anthony J. Browning, Jon J. Cartledge (2007) The Role of Urinary Kidney Stone Inhibitors and Promoters in the Pathogenesis of Calcium Containing Renal Stones beau-ebu update series5, 126–136.
[8]. Baumann jm, Affolter B, Caprez U, et al. (2001) Hydroxyapatite induction and Secondary aggregation of calcium oxalate, two important processes in calcium Stone formation. Urol Res; 29(6): 417-2.
[9]. Berglund, M., Akessson, A., Nermell, B., and Vahter, M. (1994). Intestinal Absorption of Dietary Cadmium in Women depends on Body Iron Stores and Fiber Intake. Environ Health Perspect 102, 1058-1066.
[10]. Bhuskute NM, Yap WW, Wah TM. (2009) A retrospective evaluation of Randall's plaque theory of nephrolithiasis with CT attenuation values. Eur J Radiol; 72: 470-472Borghi, L., Schianchi, T., Meschi, T. (2002) "Comparison of two diets to the prevention of recurrent stones in idiopathic hypercalciuria," N. Egl. J. Med., 346(2), pp.77-84.
[11]. Borsatti A (1991) Calcium oxalate nephrolithiasis: Defective oxalate transport. Kidney Int; 39(6): 1283-8.
[12]. Boulay I, Holtz P, Foley WD, White B, Begun FP. Ureteral calculi: diagnostic efficacy of helical CT and implications for treatment of patients. Am J Roentgenol 1999; 172:1485-90.
[13]. Chandoke PS (2002) When is medical prophylaxis cost-effective for recurrent calcium stones? J Uro/; 168: 937-0.
[14]. Chen MY, Zagoria RJ. Can noncontrast helical computed tomography replace intravenous autography for evaluation of patients with acute urinary tract colic? J Emerge Med 1999; 17:299-303.
[15]. Coe FL, Evan A, Worcester E. (2005) Kidney stone disease, J Clin Invest; 116(10):2598-8.
[16]. Colabawalla N, (1971) "Incidence of urolithiasis in India", In "Technical Reports Series No 8". Indian Council of Medical Research Division of Publication and Information, New Delhi, 42.

[17]. Curhan GC Willett WC, Speizer FE (1997) Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women Ann Inter Med 126: 497.
[18]. Curhan GC, Willett WC, Rimm EB, et al. (1993) A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med ; 328(12): 833-8.
[19]. Dalrymple NC, Verge M, Anderson KR, Bovet P, Covey AM, Rosen field AT, et al. The value of unenhanced helical computerized tomography in the management of acute flank pain. J Urol 1998; 159:735-40.
[20]. Doddametikurke RB, Biyani CS, Browning AJ, Cartledge JJ (2007) The role of urinary kidney stone inhibitors and promoters in the pathogenesis of calcium containing renal stones, EAU-EBU Update Series. 5: 126–136Evan AP, Coe Fl, Ungeman jE, et aI. (2005) Insights on the pathology of kidney stone formation. Uro/ Res; 33: 383-9.
[21]. Goldfarb OS, Fischer ME, Keich Y, (2005) A twin study of genetic and dietary influences on nephrolithiasis: a report from the Vietnam Era Twin (VET) Registry. Kidney Int; 67(3): 1053-1.
[22]. Goldfarb S. Oiet (1994) nephrolithiasis. Annu Rev Med; 45: 235-3.
[23]. Heller HJ, Ooerner MF, Brinkley LJ, et al. (2003) Effect of dietary calcium on stone forming propensity. J Uro/; 169(2): 470-4.
[24]. Hesse A, Straub M. (2006) Rational evaluation of urinary stone disease. Urol Res; 34(2): 126-0.
[25]. Hesse, Brandle E., D. Wilbert E., Köhrmann K. U., P. Alken K. U., (2003) Study on the prevalence and incidence of urolithiasis in Germany comparing the years 1979 vs. 2000. Eur Urol. 2003 Dec; 44(6):709-13.
[26]. Hiatt RA, Dales LG, Friedman GD, Hunkeler EM (1982): Frequency of urolithiasis in a prepaid medical care program. Am J Epidemiol 115: 255–265.
[27]. Hussain Billimoria, F., P. Singh, F., (1990) Urolithiasis in Northeast Bombay: Seasonal prevalence and chemical composition of stones Int. Urol. Nephrol., 22 119.
[28]. Jaeger P, Robertson WG (2004) Role of dietary intake and intestinal absorption ofoxalate in calcium stone formation. Nephron physio/; 98(2): p64-1.
[29]. Jie Ding, Na Guan, Qingfeng Fan, , Yiming Zhao, Jingqiao Lu, Yi Ai, Guobin Xu, Sainan Zhu, Chen Yao, Lina Jiang, Jing Miao, Han Zhang, Dan Zhao, Xiaoyu Liu, and Yong Yao, (2009) Melamine-Contaminated Powdered Formula and Urolithiasis in Young Children, The new england journal of medicine established in 1812 march 12, vol. 360 no. 11 Johnson CM, Wilson DM, O' Fallon WM (1979) Renal stone epidemiology: A 25year study in Rochester, Minnesota. Kidney Int; 16: 624–31.
[30]. Khan SR, Shevock PN, Hackett RL (1989) Urinary enzymes and calcium oxalateurolithiasis. J Uro/; 142: 846-9.
[31]. Knoll, T. (2007) Stone disease, Eur Urol Suppl., 6, 717-722.
[32]. Kok DJ, lestra JA, Doorenbos CJ, et a/. (1990)The effects of dietary excess in animal protein and in sodium on the composition and the crystallization kinetics of calcium oxalate monohydrate in urines of healthy men. J Clin Endocrinol Metab ; 4: 861-7.
[33]. Lee, Y., Huang, W., Huang, j. and Chang, L. (2008) Testosteron enhances where as estrogen inhibits calcium oxalate stone formation in ethylene glycol treated rats, J. Urol., 156, 502-505.
[34]. Levine JA, Neitlich J, Verga M, Dalrymple N, Smith RC. Ureteral calculi in patients with flank pain: correlation of plain radiography with unenhanced helical CT. Radiology 1997; 204:27-31.
[35]. Lingeman JE, Saywell RM Jr, Woods JR, Newman DM (1986) Cost analysis of extracorporeal shock wave lithotripsy relative to other surgical and nonsurgical treatment alternatives for urolithiasis. Med Care; 24:1151-60.
[36]. López M., Hoppe B., (2010) History, epidemiology and regional diversities of urolithiasis. Pediatr. Nephrol., 25 49.
[37]. Madore F, Willett WC, Stampfer MJ (1998) Nephrolithiasis and risk of hypertension.
[38]. Am J Hypertens; 11: 46–53 Malvinder S Parmar, medical director (2004) Kidney stones BMJ. Jun 12; 328(7453): 1420–1424.
[39]. Mandel NS, Mandel GS. (1989) Urinary tract stone disease in the United States veteran population. II. Geographical analysis of variations in composition. J Urol; 142: 1516-1.
[40]. Masarani M, Dinneen M. Ureteric colic: new trends in diagnosis and treatment. Postgrad Med J 2007 Jul; 83(981):469-72.
[41]. Massey LK, Roman-Smith H, Sutton RL (1993) Effect of dietary oxalate and calcium on urinary oxalate and risk of calcium oxalate kidney stones. J Am Diet Assoc; 93: 901-6.
[42]. Massey LK. (2003) Dietary influences on urinary oxalate and risk of kidney stones. Front Bio Sci; 8: s584-4.
[43]. Mattle D, Hess B. (2005) Preventive treatment of nephrolithiasis with alkali citrate a critical review, Urol Res; 33:73-9.

[44]. Miller, N.L. and Lingeman, J.E. (2007) Management of kidney stones, BMJ, 334 (7591): 468–72.
[45]. Mirian A. Boim, Ita P Heilberg, Nestor Schor (2010) Phyllanthus niruri as a promising alternative treatment for nephrolithiasis. Int. braz j urol, 36 (6).
[46]. Moe O. W, (2006) Kidney stones: pathophysiology and medical management. Lancet. 28;367 (9507):333-44
[47]. Moe O. W., Pearle M. S., Sakhaee K., (2011) Pharmacotherapy of urolithiasis: evidence from clinical trials.KidneyKidney Int., 79 385.
[48]. Moe OW, Abate N, Sakhaee K (2002) Normouricosuric uric acid urolithiasis: a systemic disease with defective renal acidification. Endo Clin North Am; 31: 895-4.
[49]. Mohanty, N.K., Nayak, R.L. and Patki, P.S. (2010) Safety and efficacy of an Ayurvedic formulation cystone in management of ureteric
[50]. Nabi, G., Downels, P., Keeley,F., Watson,G, and Mcccliton,S (2007) Extracorporal shack wave lithotripsy (ESWL) Vesrsus ureteroscopic management for ureteric calculi, Cochrane database 3,34-52.
[51]. Nikhil Gupta Chander J, et al. (2010) Retroperitoneal laparoscopic pyelolithotomy versus extracorporeal shock wave lithotripsy for management of renal stones. J Minimal access surgery;Oct-dec shock 6- wave lithotripsy for management of renal;6(4),106-110
[52]. Pak CYC (2004a) Rapid communication: relative effect of urinary calcium and oxalate on saturation of calcium oxalate. Kidney Int; 66: 2032-7.
[53]. Pak CYC (2004b) Medical management of urinary stone disease. Nephron Glin Pract; 98: c49-3.
[54]. Pakistan Muhammad Hassan KHASKHELI1, Syed Tufail Hussain SHERAZI2,∗ , Huma Mazhar UJAN1, Sarfaraz Ahmed MAHESAR2, Turk J (2012)Transmission FT-IR spectroscopic analysis of human kidney stones in the Hyderabad region of Chem 36 , 477 – 483. c TUB¨ ˙ ITAK doi:10.3906/kim-1108-26
[55]. Park CH. (2000) Prevalence of employer self-insured health benefits: national and state variation. Med Care Res Rev 57:340–360
[56]. Pendse K., Srivastava A. K., Kumavat J. L., Goyal A., Ghosh R., Sharma, P. P.Singh, (1984) Urolithiasis in Udaipur (Rajasthan). J. Indian Med. Assoc., 82 151.
[57]. Porena M, Guiggi P, Micheli C. (2007) Prevention of stone disease. Urol Int; 79(suppI1): 37-6.
[58]. Portis AJ, Sundaram CP. (2001) Diagnosis and Initial Management of Kidney Stones. Am Fam Physician Apr 1; 63(7):1329-38
[59]. Potts JM. (2004) Essential Urology: A guideline to clinical practice. Humana Press.p:117-130.
[60]. Prentice, A., Schoenmakers, I., Laskey, M.A., de Bono, S., Ginty, F., Goldberg, G.R., (2006) Symposium on 'Nutrition and health in children and adolescents'; Session 1: Nutrition in growth and development: Nutrition and bone growth and development The Proceedings of the Nutrition Society. 65(4) 348–360
[61]. Qiu SR, Wierzbicki A, Orme CA, Cody AM, Hoyer JR, Nancollas GH, Zepeda S, De Yoreo JJ (2004) Molecular modulation of calcium oxalate crystallization by osteopontin and citrate. Proceedings of the National Academy of Sciences 101: 1811-1815
[62]. Ramello, C. Vitale, M. (2000) Epidemiology of nephrolithiasis Marangella, Nephrol J., 13 S65.
[63]. Rizvi, S.A., Naqvi, A.A., Husssain, Zafar, M.N., Sultan,S. and Mehdi., H. (2002) Pediatric urolithiasis, developing nation perspective, Urol., 168, 1522-1525
[64]. Robertson W. G., Hughes H., yall Ed. R., Bais R., Marshal V.l, Rofe. Smith A., L, Walker V., (1994) "Epidemiology of urinary stone disease in Saudi Arabia". In "Urolithiasis", R Plenum Press, New York, 453.
[65]. Robertson WG, Peacock M, Heyburn PJ, et al. (1978) Risk factors in calcium stone Disease of the urinary tract. Br J Uro/; 50: 449-4.
[66]. Robertson WG. (2003) A risk factor model of stone-formation. Front Biosc; 8: s1330-8.
[67]. Rodgers AL, Lewandowski S (2002) Effects of 5 different diets on urinary risk factors for calcium oxalate kidney stone formation: Evidence of different renal handling mechanisms in different race groups. J Uro1; 168: 931-6.
[68]. Roehrborn C, McConnell J. (2007) Benign prostatic hyperplasia: Etiology, pathophysiology, epidemiology and natural history. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh Urology. 9th ed. Philadelphia: Saunders; p. 2727-65.
[69]. Saita A, Bonaccorsi A, Motta M. (2007) Stone composition: where do we stand? Urollnt; 79 (suppI1): 16-9.
[70]. Saltzman JR, Russell RM (1998) the aging gut. Nutritional issues. Gastro enterol Clin North Am 27: 309–324.

[71]. Sasha Stumpers and Neil Thomson, (2013) Australian Indigenous HealthInfoNet, Review of kidney disease among Indigenous people, Australian Indigenous Health Bulletin Sasha Stumpers1 and Neil Thomson1 Vol 13 No 2, April – June

[72]. Schwille PO, Mancharan M, Rumenapf G, et al. (1989) Oxalate measurement in the picomole range by ion chromatography: values in fasting plasma urine of controls And patients with idiopathic calcium nephrolithiasis. J Clin Chem Clin Biochem ; 27: 87-9.

[73]. Seitz C, Liatsikos E, Porpiglia F, Tiselius H-G, Zwergel U. (2009) Medical therapy to facilitate the passage of stones: what is the evidence? Eur Urol; 56:455–71.

[74]. Serhat. G. and Kupeli. B. (2006) Consumption of historically and current phytotheraptic agents for urolitiasis, J. Urol., 176, 450-455

[75]. Shokeir AA. Renal colic: new concepts related to pathophysiology, diagnosis and treatment. Curr Opin Urol 2002 Jul; 12(4):263-9.

[76]. Siener R, Hesse A. (2005) recent advances in nutritional research on urolithiasis. World J Uro1; 23(5): 304-8.Taylor EN, Stampfer MJ, Curhan GC. Fatty acid intake and incident nephrolithiasis. Am J kidney Dis; 45 (2): 267-4.

[77]. Singh L. B. K., Prasad S. N., Singh P. P., (1977) Urinary bladder stone disease and common types of urinary stones found in Manipur, Asian Med. J., 20 589.

[78]. Singh P. P., Singh L. B. K., Prasad S. N., Singh M. G., (1978) CHAPTER : II : Brief Review on Urinary Calculi Growth and Characterization of Struvite and Related Crystals 100Clin. Am. J. Nutr.31 1519.

[79]. Singh P., Pendse A., Rathore V., Dashora P., (1988) Urinary biochemical profile of patients with ureteric calculi in Jodhpur region (north-western India) Urol. Res., 16 105.

[80]. Smith J, Mattoo TK, Stapleton FB. Patient information: Kidney Stones in children. 2010.Up to date online. http://www.uptodate.com/patients/content/topic.do?topicKey=~W7Wuul5gemj5LrR

[81]. Soucie JM, Thun MJ, Coates RJ (1994) Demographic and geographic variability of kidney stones in the United States. KidneyInt; 46:893–99.

[82]. Sowers MR, Jannausch M, Wood C, Pope SK, Lachance LL, Peterson B (1998). Prevalence of renal stones in a population-based study with dietary calcium, oxalate, and medication exposures. Am J Epidemiol, May 15;147(10):914-20.

[83]. Srivastava T, Alon US (2005) Pathophysiology of hypercalciuria. Pediatr Nephrol 22:1659–1673[PubMed]

[84]. Stamatelou KK, Francis ME, Jones CA (2003). Time trends in the reported prevalence of kidney stones in the UnitedStates: 1976–1994.KidneyInt63:1817–23.

[85]. Strohmaier WL, Hormann M. (2000) Economics aspect of urolithiasis and metaphylaxis in Germany. In Rodgers AL, Hibbert BE, Hess B, Khan SR, Preminger GM (eds): Urolithiasis. Cape Town; 1: 406-9.

[86]. Sutherland J., Parks J., F. Coe J., (1985) Recurrence after a single renal stone in a community practice. Miner. Electrolyte Metab., 11 267.

[87]. Sutton RAL (2006) the use of risk indices: do they predict recurrence? Urol Res; 34: 122-5.

[88]. Taylor EN, Curhan GC. (2004) Role of nutrition in the formation of calcium-containing kidney stones. Nephron Physio/; 98(2): 55-3.

[89]. Taylor EN, Stampfer MJ, Curhan GC. (2005) Diabetes mellitus and the risk of nephrolithiasis. Kidney Int Sep;68(3):1230-5.

[90]. Thomas E, von Unruh GE, Hesse A. (2008) Influence of a low- and a high- oxalate vegetarian diet on intestinal oxalate absorption and urinary excretion. Eur J Clin Nutr; 62(9): 1090-7.

[91]. Tombolini. P, Ruoppolo. M, Bellorfonte. C and Follini. M (2010) Lithotripsy in the treatment of lithiasis, J, Nephrol., 13, 571-582.

[92]. Trinchieri, A., Lizzano, R., Marchesotti, F. and Zanetti, G. (2006) Effect of potential renal acid load of foods on urinary citrate excretion in calcium renal stone formers, Urol. Res., 34, 1-7.

[93]. Verkoelen CF (2006) Crystal retention in renal stone disease: a crucial role for the glycosaminoglycan hyaluronan? J Am Soc Nephrol Jun;17(6):1673-87.

[94]. Verkoelen, C.F., van der Boom, B.G., Schroder, F.H., Romijn, J.C., 1997. Cell cultures and nephrolithiasis. World J. Urol. 15, 229–235

[95]. Vieweg J, Teh C, Freed K, Leder RA, Smith RH, Nelson RH, et al. Unenhanced helical computerized tomography for the evaluation of patients with acute flank pain. J Urol 1998; 160:679-84.

[96]. Vyas Amit S, Patel Mandev B, Patel Ajay I, and Joshi Namrata R, (2012) Epidemiology of renal stone ailment in few district of Gujarat state, pharma science monitor An international journal of pharmaceutical sciences, Vol-3, Issue-2, A

[97]. Welshman SG, McGeown MG. (1975) The relationship of urinary cations, calcium, magnesium, sodium and potassium in patients with renal calculi. Br J Uro/;47: 237-2.
[98]. Worcester, Parks J. H., M. A. Josephson, R. A. Thisted, F. L. Coe, (2003) Causes and consequences of kidney loss in patients with nephrolithiasis. Kidney Int. 2003 Dec; 64(6):2204-13.
[99]. Yagisawa T, Ito F, Osaka Y, Amano H, Kobayshi C, Toma H (200)The influence of sex hormones on renal osteopontin expression and urinary constituents in experimental urolithiasis. J Urol; 166: 1078-82.
[100]. Yilmaz S, Sindel T, Arslan G, Ozkaynak C, Karaali K, Kabaalioglu A, et al. Renal colic: comparison of spiral CT, US and IVU in the detection of ureteral calculi. Eur Radiol 1998; 8:212-7.
[101]. Yoshida O., A. Terai O., Ohkawa T., Okada Y., (1999) National trend of the incidence of urolithiasis in Japan from 1965 to 1995. Kidney Int., 56 1899
[102]. Yoshida O., Okada Y., (1990) Epidemiology of urolithiasis in Japan: a chronological and geographical study, Urol. Int, 45 104.
[103]. Zahid H., Bawazir A. S., Rafiuddin Naser (2009) Plant based native therapy for the treatment of Kidney stones in Aurangabad (M.S) Journal of Pharmacognosy and PhytochemistryVolume 1 Issue 6page189-193

IOSR Journal of Pharmacy (IOSR-PHR) is UGC approved Journal with Sl. No. 5012

Uthaya Chandirika Jayaraman " Review on Uro-Lithiasis Pathophysiology and Aesculapian Discussion.” IOSR Journal of Pharmacy (IOSRPHR), vol. 8, no. 2, 2018, pp. 30-42