

1. Introduction

1.1 Kidney

The Kidneys are two small fist-sized (reddish brown) organs in human body¹, located behind the abdomen, on Either side of the spinal cord. Each kidney weight about 150 -160g and Measures 12 cm long, 5-6 cm wide, and 2.5-3 cm thick.

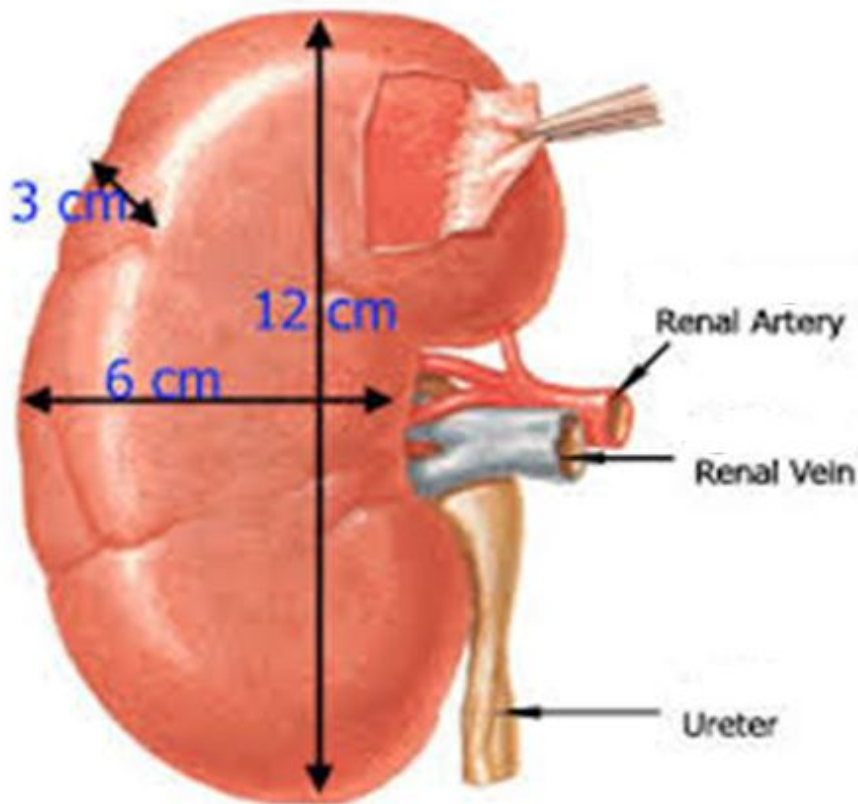


Figure 1-1: Structure of a Kidney

The kidney is one of the key organs in the urinary system, also known as the renal system, consists of six organs, two kidneys, two ureters, the bladder, and the urethra.

The right kidney slightly lower than left due to space occupied by liver². Each kidney consists of millions of functional units called nephrons (tiny filtering units). The purpose of the renal system is to eliminate wastes from the body, regulate blood volume and pressure, and regulate blood pH. The kidneys have extensive blood supply via the renal arteries which leave the kidneys via the renal vein. Following filtration of blood and further processing, wastes (in the form of urine) exit the kidney via the ureters.

1.2 Ureters

The ureters are two tubes that drain urine from the kidneys to the bladder. Each ureter is a muscular tube about 10 inches (25 cm) long. Muscles in the walls of the ureters send the urine in small spurts into the bladder. After the urine enters the bladder from the ureters, small folds in the bladder mucosa act like valves preventing backward flow of the urine. The outlet of the bladder is controlled by a sphincter muscle. A full bladder stimulates sensory nerves in the bladder wall that relax the sphincter and allow release of the urine.

1.3 Urinary Bladder

The urinary bladder is a hollow or elastic organ that sits on the pelvic floor. The urinary bladder can hold approximately 17 to 18 ounces (500 to 530 ml) of urine; however the desire to micturate is usually experienced when it contains about 150 to 200 ml. When the bladder fills with urine (about half full), stretch receptors send nerve impulses to the spinal cord, which then sends a reflex nerve impulse back to the sphincter (muscular valve) at the neck of the bladder, causing it to relax and allow the flow of urine into the

urethra. The ureters enter the bladder diagonally from its dorsolateral floor in an area called the trigone. The trigone is a triangular shaped area on the postero-inferior wall of the bladder. The urethra exits at the lowest point of the triangle of the trigone. The urine in the bladder also helps regulate body temperature. If the bladder becomes completely void of fluid, it causes the patient to chill.

1.4 Urethra

The urethra is a muscular tube that connects the bladder with the outside of the body. The function of the urethra is to remove urine from the body. It measures about 1.5 inches (3.8 cm) in a woman but up to 8 inches (20 cm) in a man. Because the urethra is so much shorter in a woman it makes it much easier for a woman to get harmful bacteria in her bladder this is commonly called a bladder infection or a UTI is E-coli from the large intestines that have been excreted in fecal matter.

The kidney generates 180 liter of filtrate a day, while reabsorbing a large percentage, allowing for the generation of only approximately 1-2 liters of urine in a healthy human. The female and male urinary system are very similar, differing only in the length of the urethra³.

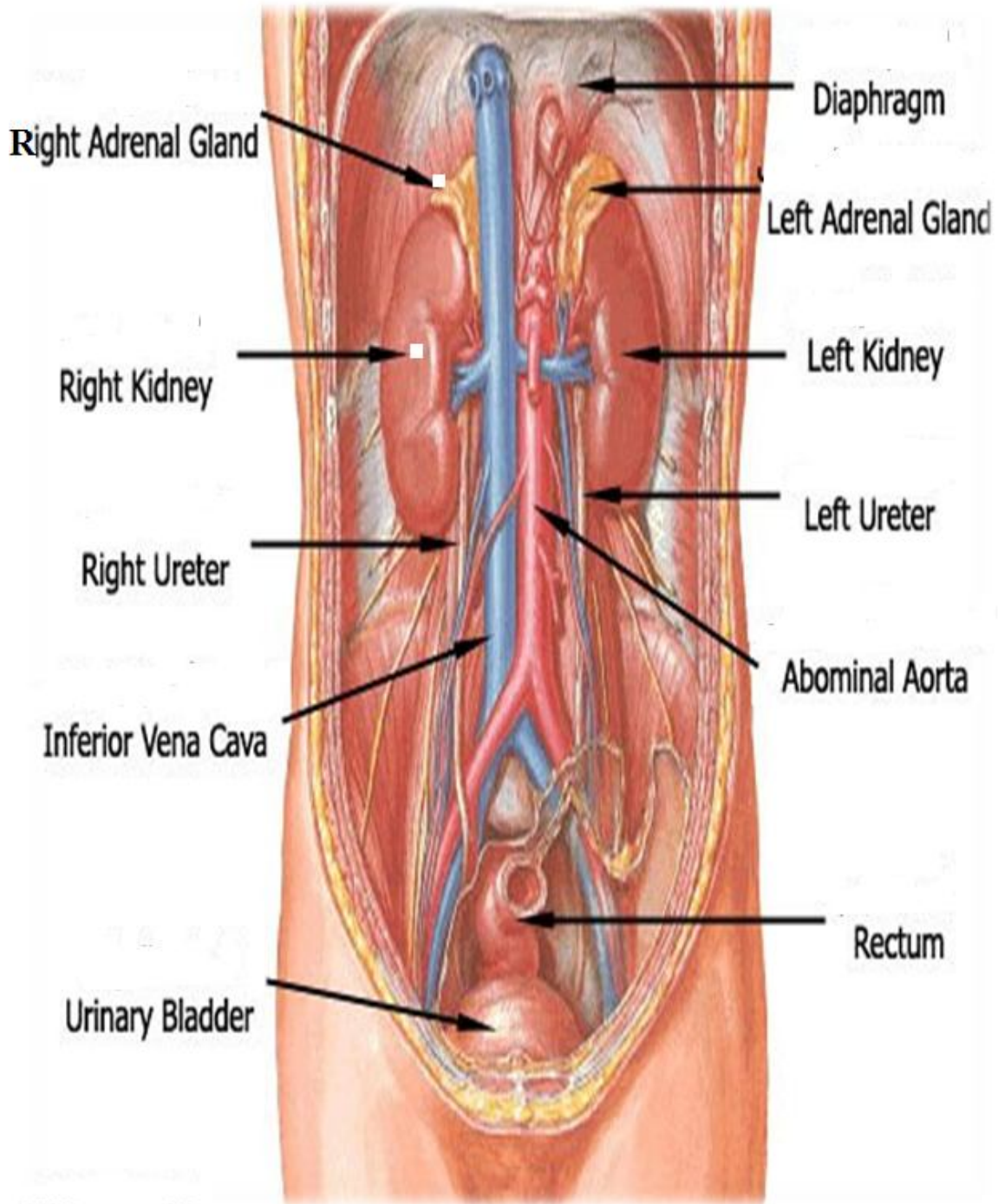


Figure 1-2: Location of the kidney in the body

1.1.1 Kidney stones diseases

Kidney stone disease or known as nephrolithiasis is a common problem especially in industrialized nations, which resulted in the death of the majority of patients^{4,5}. It is defined as one or more stones namely aggregate of crystals mixed with protein matrices, which are formed in the kidney or in the ureter. Kidney stones are small, hard deposits of mineral and acid salts on the inner surfaces of kidneys. Normally, the substances that make up kidney stones are diluted in the urine. When urine is concentrated, such substances stick to gether , solidify and remain in in the kidney resulting in a kidney stone⁶⁻⁸ This may cause obstruction of urine flow in the renal collecting system, ureter or urethra which causes severe pain, bleeding or local erosion of kidney tissue ⁹.

Kidney stone disease affects 1to 20 % of the general population. According to data provided by the U.S. National Health Interview Survey (1990 -1992) approximately 1 million people suffered from stone disease yearly. In Asia, its lifetime incidence is 2 - 5% ¹⁰.

The incidence and prevalence of kidney stone also varies in proportion to age, race and gender. Kidney stone disease afflicts both men and women but with higher prevalence in men than in women. The lifetime chance of an individual having a stone is 10 - 15% and the peak age of onset is 20 - 30 years old ¹¹. The risk of recurrence is 74% within 10 years for the first-time stone formers and therefore increasing the risk of permanent kidney damage despite modern techniques of stone removal.

The size, shape, hardness and general appearance of the kidney stone vary depending on the individual case. Although kidney stones are composed of

many different compounds, there is one common property among them : they all form solid salts¹².

1.1.2 Classification of stones

Classification of urinary stones according to their chemical composition is an important requirement for proper management of the disease.

Quantitative chemical analysis of the urinary stones has been preferred by many investigators. particular importance are micro analytical techniques used for stones below 5 mg in weight ^{13,14}. Almost all these investigators apply calculations, based on certain assumptions, According to the chemical analysis findings to arrive for the composition of compounds. several classifications of urinary stones have been suggested ¹⁵⁻¹⁷,

The chemical composition of kidney stone is quite varied, some are inorganic compounds such as calcium phosphate and some are organic salts such as calcium oxalate. Others are non-salt types of organic compound such as uric acid and cystine ¹⁸

1.1.2.1 Calcium stones

One of the Stone Types is Calcium stones. Calcium contain from insoluble crystals ¹⁹. form which are commonly either hydrates of calcium oxalate, Calcium Oxalate Monohydrate $\text{CaC}_2\text{O}_4\cdot\text{H}_2\text{O}$, and Calcium Oxalate Di hydrate $\text{CaC}_2\text{O}_4\cdot 2\text{H}_2\text{O}$, approximately 80% of all kidney stones are calcium. Calcium stones are generally a mixture of calcium phosphate and calcium oxalate precipitate, depending on the main constituent of the stone, we call them either calcium oxalate or calcium phosphate stone. In the majority of calcium kidney stones, calcium oxalate is the main constituent and calcium phosphate precipitate is present in amounts more than 90% calcium oxalate

with trace amounts of calcium phosphate (the proportion of calcium phosphate in stones has increased over time) ²⁰⁻²⁵.

high urinary calcium is a risk factor for recurrent stone disease^{26,27}.

Calcium stones can typically be seen on plain x-ray. Usually, no specific cause is found on why these stones develop, however they can occur in certain medical conditions, and in several types of kidney disorders. the composition of the stones differ a little by the location in which they are formed ^{4,5, 28, 29}.

Calcium plays an essential role throughout the body ³⁰. Although high dietary calcium had been strongly suspected of raising the risk of stone disease in the past, a recent cohort study of more than 50,000 male health professionals aged 40 to 75 years, has shown that very low calcium intake can actually predispose to kidney stone formation as well^{31,32}.

1.1.2.2 Phosphate stones

Five different phosphates, namely, hydroxyapatite _HAP. carbonate apatite, brushite, whitlockite, and struvite individually or in a mixture, have been detected as either major or minor components of human renal calculi ^{33,34}. The thermodynamically stable phase in contact with the aqueous Ca]PO₄]Mg system is brushite at pH values not exceeding approximately 5 and hydroxyapatite at pH=5 ^{35,36}. Therefore in such a system other calcium phosphates finally transform, according to prevailing conditions, into one or another by a solution mediated process. Conversion of brushite to hydroxyapatite seems to be a slow process under physiological conditions though even the opposite has been reported ³⁷⁻³⁹. Inhibition of calcium phosphates crystallization has also been studied. Magnesium inhibits crystallization of hydroxyapatite ^{40,41} but exerts no influence on brushite ^{42,43}. Two main categories of phosphate containing stones can be distinguished:

calcium phosphate stones and the so-called struvite infection stones. The former calculi are basically composed of hydroxyapatite or brushite and the later are comprised of struvite⁴⁴. A more detailed classification shows that 9.5% of all stones are mainly formed by hydroxyapatite, 2.1% by brushite and 14.6% by struvite⁴⁵. struvite stone (magnesium phosphates, ammonium and sodium salts). Infection stones form in the setting of upper urinary tract infection with urease-producing bacteria. Those microorganisms hydrolyze urea producing ammonia and hydroxide, increasing urinary pH and phosphate that bind to magnesium to form a “triple-crystal” composed of struvite (magnesium ammonium phosphate) and/or calcium carbonate apatite. Those calculi usually grow as branched stones that occupy a large portion of the collecting system, namely, staghorn calculi⁴⁶.

1.1.2.3 Uric acid stone

About 5–10% of all stones are formed from uric acid⁴⁷. People with certain metabolic abnormalities, including obesity⁴⁸, may produce uric acid stones. Uric acid stones may form in association with conditions that cause hyperuricosuria (an excessive amount of uric acid in the urine) with or without hyperuricemia (an excessive amount of uric acid in the serum). They may also form in association with disorders of acid/base metabolism where the urine is excessively acidic (low pH), resulting in precipitation of uric acid crystals. A diagnosis of uric acid urolithiasis is supported by the presence of a radiolucent stone in the face of persistent urine acidity, in conjunction with the finding of uric acid crystals in fresh urine samples⁴⁹.



1.1.2.4 cystine stone


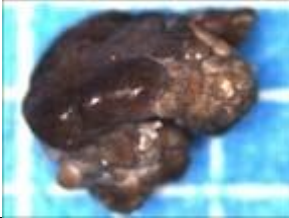
Cystine stones are produced by an inherited disorder (genetic disorder) of the transport of amino acid cystine that results in excess of cystine in the urine (cystinuria). Cystine calculi in urinary tract present a significant problem in patients. We have recorded that cystine calculi are very uncommon in our region. Cystine crystals are unusually identified in the urinary deposits⁵⁰⁻⁵³.



1.1.2.5 xanthine stone



Xanthine stone in small amounts.


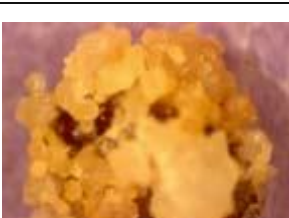
In urinary stone analysis, the Hospital laboratories relied only on the simple qualitative and semi- quantitative chemical analytic techniques ⁵⁴. which only give arbitrary information on stone composition ^{55,56}. However, many investigators appreciated the value of quantitative chemical analytic techniques and several schemes for the classification of urinary stones were suggested ^{57,58}.

	
Calcium Oxalate Monohydrate deposited over Silica	Calcium Oxalate Monohydrate

	
Calcium Oxalate Monohydrate (coated with Triamterene)	Calcium Oxalate Monohydrate

	
Calcium Oxalate Monohydrate	Calcium Oxalate Dihydrate

	
Carbonate Apatite	Brushite

	
Struvite	Struvite (Ferret)

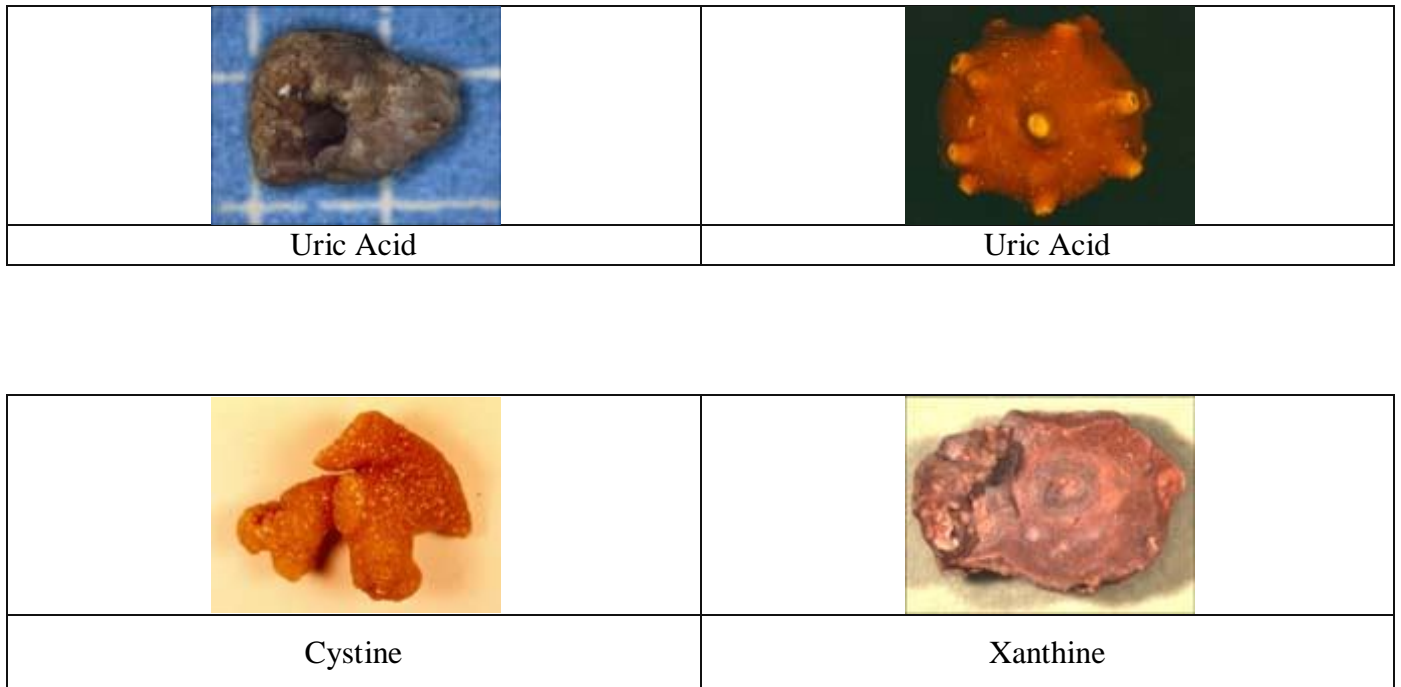


Figure 1-3: Kidney Stones Photographs

1.1.3 Causes of kidney stone

There are no definite reasons for the formation of kidney stones .. In some cases, urinary calculus may be predicted from the following risk factors; 24 hour urinary pH, amount of calcium (Ca), oxalate and uric acid excreted and level of urinary inhibitors⁵⁹, in addition to the possible role of diet, Other diseases Cystinuria is a condition where lot of amino acid cystine is deposited which do not dissolve in the urine and thus lead to stone formation drinking water, in the last decade due to wrong food habits ^{60,61}.

1.1.3.1 Urinary pH.

In controls, the 24 hour urinary pH is higher than patients with urolithiasis though the difference may be insignificant .Therefore, low urinary pH is

considered as a risk factor,⁴¹ particularly below the dissociation constant of uric acid ⁶²⁻⁶⁶.

1.1.3.2 HyperCalciuria

HyperCalciuria is considered when the 24 hour urinary Ca content is above the upper limit of normal which is 300 mg in male's and 250 mg in females)⁶⁷, as the relative risk of stone formation increased with increasing urine Ca level and concentration ^{68,69}. Therefore, in patients with stone recurrence, strong enhancement of Ca Excretion⁷⁰, and hyperCalciuria is markedly more frequent than in first stone formers⁷¹. It is reported that more than half of both men and women with recurrent stone formation have hypercalciuria⁷². In Saudi Arabia and Abu-Dhabi, hyperCalciuria accounts for 9-29% of patients with

Urolithiasis ⁷²⁻⁷⁵. However, a higher percentage than that and up to 81% of patients with urolithiasis is stated in current western reports ^{69, 64,74,76-80}. However, in controls, hyperCalciuria is less commonly reported and at a lower relative frequency percent than in patients^{62, 64}. Therefore, it seems that hyperCalciuria is a risk factor in the presence of other urinary disturbances as change in urinary pH^{62, 68, 80, 81}, low urinary volume as a specific abnormality or hyperuricosuria^{72, 80}.

1.1.3.3 Hyperuricosuria

is considered when the 24 hour urinary uric acid content is 5000 μmol or more and a lower level was also reported. More frequently, uric acid is evaluated in mg and hyperuricosuria then will be considered when the 24 hour urinary uric acid content exceeds 800 mg in men and 750 mg in women. tubular acidosis which is associated with hypercalciuria and hypocitraturia ⁸², and some genetic alterations, which are associated with

hyperoxaluria (Hyperoxaluria is considered when the 24 hour urinary oxalate content exceeds the upper limit of normal which is 40 mg. Also an upper limit of normal higher or lower than that was considered) hypercystinuria and hypercalciuria⁸³⁻⁸⁵.

1.1.3.4 Hyperoxaluria

Hyperoxaluria is considered when the 24 hour urinary oxalate content exceeds the upper limit of normal which is 40 mg^{62,77}. Also an upper limit of normal higher or lower than that was considered^{86,87}. Idiopathic Ca oxalate urolithiasis is a frequent and recurrent multifactorial disease. In patients with Ca oxalate stones (monohydrate or mixed mono and dihydrate), hyperoxaluria in 24 hour urine was the most common abnormality after hypocitraturia⁷¹.

1.1.3.5 Some Ionic Correlations

A. Magnesium, calcium, potassium.

In controls, in the 24 hour urine, magnesium (Mg) shows prominent direct correlation with uric acid, oxalate and phosphate⁶². Meanwhile, Ca shows no correlation with Mg²¹ and an obvious direct correlation with uric acid^{62,88}. Thus leading to a low urinary Ca/Mg ratio in the controls^{62,89}. Furthermore, in the controls, the 24 hour urinary potassium (K), shows direct correlation with phosphate, uric acid and Ca but not oxalate⁶². On the other hand, in patients with urolithiasis, the 24 hour urinary Ca shows prominent direct correlation with uric acid, and oxalate^{60,64,73,90}. However, phosphate show prominent correlation with Mg more than Ca Thus leading to an increase in the Ca/Mg ratio in these patients especially in those with hyperoxaluria, hyperuricosuria, or both^{62,74} In addition, the direct correlations between Ca and oxalate in the 24 hour urine of stone formers is well represented in the

Ca stone composition⁶². Meanwhile, it may be attributed to the presence of malondialdehyde (MDA, one of the urinary lipid peroxides) in the urine of patients which show correlations with both oxalate (significantly linear correlation) and Ca (negative linear correlation)⁶¹. Furthermore, in patients with urolithiasis, the 24 hour urinary K shows more correlations with phosphates than oxalate or uric acid and no correlation with Ca⁶².

Therefore, it was reported that the 24 hour urinary Mg level is lower in patients with urolithiasis than controls although the difference is statistically insignificant.^{61, 68, 71} On the other hand, higher ranges of

24 hour urinary K, were reported in controls more than in patients with urolithiasis ⁶⁷. In addition, after extracorporeal shock wave lithotripsy (ESWL), the mean 24 hour urinary K was lower in patients with stone growth than in those without stone growth.⁹¹

B. oxalate, phosphate.

In controls, in the 24 hour urine, uric acid shows a direct correlation with phosphate and oxalate^{62, 88}. However, its correlation with phosphate is far more than that with oxalate. However, in patients with urolithiasis, the 24 hour urinary uric acid shows prominent direct correlation with oxalate far more than with phosphate. This correlation is presented in the uric acid stone composition by the presence of variable amounts of oxalate (<40%) and only trace amount of phosphate⁶². Meanwhile, in the 24 hour urine of stone formers, there is a mutual direct correlation between oxalate and phosphate⁶². This correlation is well presented in the composition of phosphate stones by the presence of variable amount of oxalate (<40%)⁵⁷.

1.1.3.6 Correlations with family history of stones.

Family history of stones is frequently reported in patients urolithiasis with.^{62,64,68, 92-96} Therefore, it is denoted that a family history of stones substantially increases the risk of stone formation in their siblings^{68,95}. Furthermore, patients with urolithiasis, hypercalciuria and hyperuricosuria show prominent correlations with family history of stones^{66,638}. Meanwhile, in the siblings of patients with Ca renal stones, hypercalciuria is considered as one of the reasonable predictors for those who are at risk of stone formation in both genders⁶⁸. In addition, in patients with urolithiasis and family history of stones, the incidence of recurrence is higher than in those without a family history of stones^{62,94,9762,94,97}. Therefore, family history of stones is considered as one of the 8 items in the stone recurrence predictive score⁹⁸.

However, in many cases it is not possible to clearly identify the underlying disorder. Indeed, in nearly all renal calculi cases, crystal formation is attributable to a combination of diverse factors that may or may not be associated with an underlying disorder. These factors can be classified into two main groups: urine composition factors and renal morphoanatomy factors.

The size of the kidney stone varies from small, medium to large. The stones found in the kidney are brown, yellow or other color. Some stones may be smooth and brittle while some of them are hard.

Kidney stones sometimes may block the urinary track and thereby cause pain while passing urine. This has been one of the disorders present in human beings for centuries. As years pass by, the number of people suffering from this problem of kidney stones has shown a steady increase. There are several risk factors studied in this disorder. major factors related to

stone formation as a result of metabolic acidosis⁹⁹⁻¹⁰¹. Stone formation is associated with increased rates of chronic kidney disease^{102,103} that may lead to renal loss⁴⁴. in the last decade due to wrong food habits^{60, 61}.

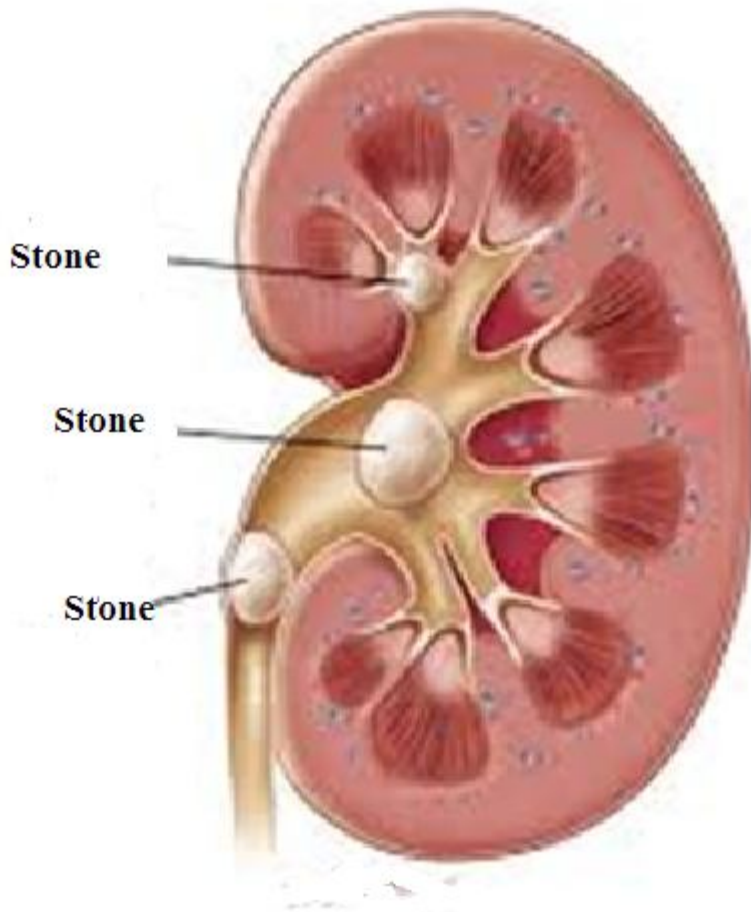


Figure 1-4: photograph of Stones in kidney

1.1.3.7 Drinking water

The possible correlation between the drinking water and prevalence of urolithiasis was considerably investigated^{62,104-107}. There is no evidence of any rise in the risk of stone formation in relation to tap water hardness^{62, 104} and underground water in the Western Region of Saudi Arabia⁶².

Meanwhile, drinking of soft water alone or with an additional factor was associated with high prevalence of urolithiasis. However¹⁰⁷⁻¹⁰⁹, it was reported that in patients with urolithiasis, drinking soft water was not associated with any changes in the urinary parameters¹¹⁰. In addition, whether in patients with urolithiasis or normal subjects^{92,93,110} drinking bicarbonate alkaline water with a high content of Ca (370-380 mg/L) leads to an increase in the urinary Ca by 50% in patients⁹⁸ and approximately 80 mg/day in normal subjects¹⁰⁶.

Furthermore, in patients with urolithiasis, drinking mineral water with high sulphate and intermediate Ca content (123.9 mg/L)¹⁰⁵ or the replacement of one litre of the usual fluid intake with mineral water in normal subjects¹⁰⁸, elevated the urinary Ca as well. Meanwhile, the presence of bicarbonate radicle in drinking water leads to an increase in the urinary citrate level whether in normal subjects or patients with urolithiasis.^{105, 106, 110} In the former group the Ca/citrate ratio was constant while in the latter it was increased¹¹⁰. In addition, drinking water with high or intermediate Ca content, raised urinary oxalate, increased osmolar excretion and significantly changed the urinary saturation in normal subjects⁹³ while in patients with urolithiasis,

The urinary excretion of oxalate either remained unchanged¹¹⁰ or significantly decreased with tendency of an increase in the urinary uric acid excretion¹⁰⁵. However, drinking low Ca content water (<20 mg/L) in patients with urolithiasis no changes in any of the urinary parameters were observed¹⁰⁷, while in normal subjects, a rise in urinary oxalate and significant decrease in urine osmolality were reported¹⁰⁶. Accordingly, contrary to what was suggested¹¹¹, there is a possible correlation between the

drinking water types and prevalence of urolithiasis. Therefore, whether in patients with urolithiasis or normal subjects, drinking hard water should be avoided due to its effects on the urinary risk factors^{105, 106, 110}. Meanwhile, in patients, for increasing urinary volume to prevent stone recurrence the use of low Ca content water or tap water is recommended^{106,110}.

1.1.3.8 wrong food habits

The large geographical variation in the incidence of renal stone disease was correlated with social and economic conditions^{94,112}. In Europe, North America, Australia, Japan and Saudi Arabia, affluence has spread to all social classes and people have tendency to eat a large quantity of rich food particularly the Saudi diet is over rich in protein and fat^{62, 113}. Meanwhile, upper urinary tract stones are more frequent among affluent people with high animal protein consumption^{104,112}. Furthermore, the risk of stone formation increased significantly with increasing body mass index among both men and women with urolithiasis^{104, 114,115}. Accordingly, the mean body mass index in patients with urolithiasis was significantly higher than that of controls^{62,79,115,116}. Although in Japan obesity is a risk factor for stone formation only in males¹¹⁵, in Saudi Arabia, it is a risk factor more common in females than males⁶². Meanwhile, as the dietary and nutritional elements are important risk factors to the etiology of urinary calculi we will consider them as follows¹⁰⁴:

A. Dietary animal protein.

In patients with urolithiasis, the mean daily intake of dietary animal protein was significantly higher than that in controls^{62,64,79}. Less commonly, the difference in the mean protein intake between patients and controls is

insignificant^{117,118}, and the mean protein intake in patients is low or even lower than that in controls⁶². Mostly the high intake of dietary animal protein was directly associated with the risk of stone formation..^{104,112,119-121}

B. Dietary fat.

In patients with urolithiasis, the mean daily intake of fat was significantly higher than that in controls^{62, 117}. Meanwhile, in patients, it is reported that the daily intake of fat was higher in men than women and the difference was statistically highly significant¹²²

C. Energy.

In patients with urolithiasis, the mean of total daily intake of energy was commonly significantly higher,^{62, 117} less commonly lower than that of controls.^{62, 79} Furthermore, in young women, sucrose intake showed relative risk of stone formation^{122, 123}. In accordance with this, in animals, the deposition of Ca oxalate in the kidney was the greatest with sucrose, fructose, sorbital and the least with glucose¹²³.

D. Dairy products and calcium supplements.

The dietary Ca intake is inversely associated with the risk of kidney stones^{95, 120, 121, 122,124-125}. Meanwhile, there is no evidence of any rise in the risk of stone formation in relation to dietary Ca intake⁹¹.

Accordingly, in patients with urolithiasis, the mean dietary Ca intake was commonly lower,^{60,62, 77, 117} less commonly significantly higher than that of controls. **57** However, the intake of supplemental Ca was positively associated with risk of stone formation in women when consumed without meals¹²². Otherwise, in patients with urolithiasis, it is recommended in a daily dose of at least 800 mg/day to prevent negative Ca balance with bone mineral loss and the increased intestinal absorption of oxalate.^{120, 125-127} As the intestinal absorption of oxalate depended linearly on the Ca

intake^{126,128}, it is reported that Ca is the most effective in reducing the urinary excretion of oxalate^{129,130}. However, rise in urinary oxalate with drinking water high (370 mg) or low (<20 mg) in Ca content was observed in normal volunteers¹⁰⁶. Meanwhile, univariate linear regression analysis revealed a non-significant association between dietary Ca and urinary oxalate in patients with urolithiasis of both genders¹²³

E. Magnesium and potassium.

In patients with urolithiasis and hyperabsorptive hypercalciuria, oral supplementation of Mg is favorable as it decreases Ca absorption and increases Mg absorption which as an inhibitor reduces risk factors of the disease¹³¹. However, K intake was found to be inversely related to the risk of stone formation¹¹⁹. Meanwhile, multiple linear regression analysis demonstrated that for each 10 mmol decrease in dietetic K intake, there was a corresponding 0.2 mm increase in stone growth¹¹¹.

F. Vitamins.

It was found that, in both men and women, there are no correlations between the risk of stone formation and the intake vitamins B6 or C when taken in large doses^{132,133}.

G. Dietary habits as risk factors.

Hyperuricosuria and other multiple urinary disturbances were common in patients with the highest; body mass index, daily intake of protein, fat, energy, Ca, fibres and vitamins^{62,134}. In accordance with this is the results of multiple linear regression analysis which revealed significant positive relationship between body mass index and uric acid, sodium, ammonium and phosphate excretion together with an inverse correlation with urinary pH in both gender and urinary excretion of Ca only in men and oxalate only in women¹³⁵. However, hypercalciuria and urinary disturbances other than

hyperuricosuria were common in patients with body mass index higher than that of controls but significantly lower than that of previously mentioned patients. Meanwhile, their daily intake of protein, energy, fibres, Ca and vitamins were significantly lower than that of controls^{62,135}. However, their daily intake of fat was significantly higher than that in controls.⁶²Therefore, as partial regression analysis revealed a weak but statistically significant relation between fat intake and urinary uric acid only in women¹²¹, it is possible that dietary fat has a more important role in stone formation than has been previously recognized. Accordingly, quantitative as well as qualitative dietary modifications especially for Ca, animal protein, fat and minerals may play an important role in reducing the likelihood of recurrent stone formation¹³⁶.

1.1.4 Symptoms of kidney stones

Kidney stones typically leave the body by passage in the urine stream, and many stones are formed and passed without causing symptoms. If stones grow to sufficient size (usually at least 3 millimeters, they can cause obstruction of the ureter.

Most the kidney stones do present themselves with many symptoms. However, if the size of the stone is large enough, then it could lead to blockage in the urinary tract resulting in severe pain while passing urine. In such condition, the person may feel pain in the lower abdomen. He may feel nausea accompanied with vomiting.

Sometimes Blood may be seen in the urine (bleeding) This is because the stone will irritate the ureter and cause blood. However all the cases with blood in urine do not really indicate the presence of Kidney stones. Some other reasons may also cause blood spots in urine.

Frequent and painful urination may also be a symptom of the presence of kidney stone. Many people feel stinging or burning sensations while passing urine. Tenderness in kidney, abdomen and Urinary tract infection may also be signs of kidney stones.

If there is a foul smell along with pus in urine, then there is a strong indication that there is a stone present in the kidney. If all these symptoms and chills persist along with any of the above symptoms then the person should seek medical help immediately before the kidney failure.

1.1.5 Treatments for kidney stones

1.1.5.1 Water and Juices

It is a major factor in uric acid lithiasis as because the urine is considered in a state of supersaturation with uric acid¹³⁷, in addition to being below the increase of the inhibition index for Ca oxalate crystal growth¹³⁸. citrate, which can slow the growth of calcium crystals¹³⁹. Citrus juices rich sources of potassium and citrate (orange and grapefruit).

1.1.5.2 Drug Treatment

Thiazide

Thiazide lowers urine calcium resulting in a fall in calcium oxalate and calcium phosphate supersaturation. Reduction of calciuria is attributed to enhanced reabsorption of calcium on the renal distal convolute tubule but very recent and compelling data show that enhanced passive Ca²⁺ transport in the proximal tubule rather than active Ca²⁺ transport in distal convolution explains thiazide-induced hypocalciuria¹⁴⁰. Doses of either chlorthalidone or hydrochlorothiazide should be no more than 25 mg/day to avoid adverse effects. Indapamide, a thiazide-like agent is also effective.

Allopurinol

Allopurinol blocks uric acid production, reducing heterogeneous nucleation of calcium oxalate by both uric acid and monosodium urate. In addition, the adsorption of normally occurring macromolecular inhibitors of calcium oxalate crystallization by uric acid or monosodium urate could be possibly averted when using this drug. However, Allopurinol (100 to 300 mg/day) is indicated only when hyperuricosuria is the only metabolic abnormality. On the other hand, alkali therapy with potassium citrate may also be beneficial, since raising urinary pH will help solubilizing uric acid converting it into potassium urate.

Potassium citrate

Potassium citrate reduces urinary saturation of calcium salts by complexing calcium and reducing ionic calcium concentration. Due to its alkalinizing effect, it also increases the dissociation of uric acid, lowers the amount of poorly soluble undissociated uric acid, reducing the propensity to form uric acid stones. The induced decline of urinary calcium during the early period of treatment represents a potential additional advantage of the drug. Therefore, potassium citrate seems to be effective in conditions of hypocitraturia, hypercalciuria, or hyperuricosuria and also in distal RTA patients, due to the need of alkalinization in the latter. Potassium citrate is preferable to sodium citrate in the prevention of urolithiasis, in doses ranging from 30 to 60 ml/day. However, adverse effects of gastrointestinal origin including epigastric pain, abdominal distention or diarrhea are common. Promising results with the use of other *citrate salts* such as potassium-magnesium, not yet approved by the Food and Drug Administration, have also been shown.

Other therapeutic agents

Potassium-acid phosphate and magnesium hydroxide were shown to have little or no effect on prevention of stone formation. A neutral potassium phosphate preparation was shown to be better than placebo in reducing calcium excretion and raising urinary inhibitors of stone formation, hence inhibiting CaOx crystal agglomeration and spontaneous nucleation on brushite¹⁴¹. also suggested a nonselective therapy, based on evidences from some of the pharmacological trials, about the beneficial and protective effects of drugs in stone recurrence rates observed in patients not categorized according to different urinary derangements hence not being influenced by the baseline urinary chemistry. Overall, potassium citrate represents the most suitable drug for such unselective treatment because of its indications for hypocitraturic, hypercalciuric, hyperuricosuric and dRTA patients. On the other hand, identification of abnormal risk factors for urinary stones is still important to rule out secondary causes of nephrolithiasis, such as cystinuria, hyperoxaluria, renal tubular acidosis and infection stones ¹⁴¹. Among all of these examples, cystinuria, the rarest, represents the single entity for which an actual specific therapy with cystine-binding thiol drugs to solubilize cystine (alphamercaptopropionylglycine or tiopronin, d-penicillamine or angiotensin converting enzyme inhibitors) would be warranted, despite the need for a vigorous increase in the amount of fluid intake and alkalinizing therapy with potassium citrate as well. Treatment of primary hyperoxaluria consists of pyridoxine, which facilitates the conversion of glyoxylate to glycine. In cases of mild, non-genetic secondary hyperoxaluria, in addition to dietary manipulation, there have been new therapeutic perspectives concerning the use of intestinal colonization with the oxalatedegrading bacteria *Oxalobacter formigenes* or other lactic-acid bacteria ¹⁴². The single

contraindication for potassium citrate would be urinary tract infection because of the alkalinizing properties of the compound. Antibiotics should rather be prescribed in such cases. Complete removal of struvite infection stones (staghorn calculi) is an important goal to eradicate causative organisms, relieve obstruction, prevent further stone growth and associated infection and preserve kidney function. The use of acetohydroxamic *acid*, a bacterial urease inhibitor, may help to reduce struvite calculi growth but the prevalence of adverse reactions is very high. The treatment of Primary Hyperparathyroidism is surgical.

1.1.5.3 Surgery

surgery is one of the common methods used to remove the stone. Surgery is usually needed if the stone is too large to pass on its own, or the stone is growing, or the stone is blocking urine flow and causing an infection or kidney damage.

Laparoscopy is one of the methods of minimally invasive surgery (MIS) that can be useful in different surgery operations^{143,144}. This method of surgery has a lot of advantages in comparison with the traditional open surgery method such as less pain, less infection, less time of recovery, etc¹⁴⁵. In contrast with these valuable advantages, a significant disadvantage of this method is missing a considerable amount of surgeon's tactile sensing that is exploited to recognize different organs and tissues^{146,147}.

1.1.5.4 Extracorporeal shock-wave lithotripsy

Extracorporeal shock-wave lithotripsy is used to remove stone slightly smaller than a half an inch that are located near the kidney. This method uses ultrasonic wave or shock waves to break up stones. Then, the stones leave the body in the urine.

1.1.6 Analysis of kidney stone

Analysis of the kidney stone is important because it allows the investigator to characterize accurately the chemical conditions prevailing at the time of nucleation and growth. No one method is sufficient to provide all the clinically useful information on the structure and composition of kidney. Thus the frequently used analytical techniques are IR^{148,149}, and techniques using X-rays, e.g. diffraction analysis(XRD)¹⁴⁸ or X-ray fluorescence¹⁴⁹. also applied for the determination of the total elemental content¹⁴⁸. In addition, atomic absorption and inductively coupled plasma(ICP)spectrometry with both optical and mass spectrometry(MS) detection have been employed for bulk analysis¹⁵⁰⁻¹⁵².

Chemical analysis therefore remains the most convenient procedure for routine use. The method is relatively rapid will detect minor components of mixed calculi and can readily be made quantitative¹⁵³

1.1.6.1 Inductively coupled plasma mass spectrometry (ICP-MS)

Inductively coupled plasma/optical emission spectrometry (ICP/OES) is a powerful tool for the determination of metals in a variety of different sample matrices (has been used for urinary stones analysis)¹⁵⁴.

1.1.6.2 FTIR

FTIR spectroscopy has been used for urinary stones analysis. The routine, easy and rapid measurements give unambiguous information about the stone composition. Specially a precise wavelength scale of the Fourier method is helpful here. A relatively good spatial resolution is important as very often

the stones are composed of core and various layers of different chemical composition¹⁵⁵.

1.1.6.3 X ray diffraction

X-ray diffraction patterns of the samples were measured in order to obtain the phase composition of the renal calculi.

1.1.6.4 U.V

Ultraviolet/visible spectroscopy involves the absorption of ultraviolet/visible light by a molecule causing the promotion of an electron from a ground electronic state to an excited electronic state of the samples were measured in order to obtain the phase composition of the renal calculi.

1.1.7 previous studies

1.1.7.1 Fredric L Coe, Andrew Evan, Elaine Worcester “ Kidney stone disease”(2005)

About 5% of American women and 12% of men will develop a kidney stone at some time in their life, and prevalence has been rising in both sexes. Approximately 80% of stones are composed of calcium oxalate (CaOx) and calcium phosphate (Cap) 10% of struvite (magnesium ammonium phosphate produced during infection with bacteria that possess the enzyme urease), 9% of uric acid (UA); and the remaining 1% are composed of cystine or ammonium acid urate or are diagnosed as drug-related stones. Stones ultimately arise because of an unwanted phase change of these substances from liquid to solid state. Here we focus on the mechanisms of pathogenesis involved in CaOx, Cap, UA, and cystine stone formation, including recent developments in our understanding of related changes in human kidney tissue and of underlying genetic causes, in addition to current therapeutics.

1.1.7.2 Abboud, I.A., Concentration effect of trace metals in Jordanian patients of urinary calculi, Institute of Earth and Environmental Sciences, Al al-Bayt University, Al-Mafraq, Jordan(2007).

Due to the increase in the number of urinary calculi disease cases in Jordan, stone samples were collected from patients from various Jordanian hospitals (Princes Basma (PBH), King Abdullah University (KAUH), Al-Basheer (ABH) and Al-Mafraq (AMH)). This study concentrates on the effect of trace metals in patients of urinary calculi. Trace metals were detected in 110 urinary calculi samples using X-ray fluorescence (XRF) and atomic absorption spectroscopy (AAS) techniques. Of the calculi examined, 21 were pure calcium oxalate (CaOax), 29 were mixed calcium oxalate/uric acid, 23 were mixed calcium oxalate/phosphate (apatite), 25 were phosphate calculi (apatite/struvite), five were mixed calcium oxalate monohydrate/struvite, four were urate calculi (mixed ammonium acid urate/sodium acid urate) and three were pure cystine calculi. The concentration measurement of Ca and other trace metals levels has been found useful in understanding the mechanism of stone formation and in evaluating pathological factors. It has been found that Ca is the main constituent of the urinary calculi, especially those stones composed of calcium oxalate and calcium phosphate. The concentration of most of the trace metals that were analyzed was (Ca = 48.18, Na = 1.56, K = 0.9, Mg = 3.08, Fe = 1.17, Al = 0.49, Zn = 0.7, Cu = 0.19, Mn = 0.029, P = 10.35, S = 1.88, Sr = 0.306, Mo = 0.2, Cr = 0.146, Co = 0.05, Ni = 0.014)%. In conclusion, metals concentration in Jordanian patient's urinary calculi samples was higher

than its equivalents of other patients'. It has been noted that there is no concentration of toxic trace elements (like Li, V, Pb, Cd, and As). Some heavy metals, however, were detected Mo, Cr, Co and Ni as traces. P and S ions are present in few calculi stones as traces.

1.1.7.3 Eimorn, Mairianga, Petcharakorn, Hanpanicha, Pote Sriboonlueb, Proton magnetic resonance spectroscopy of the kidney in renal stone disease., October, 20 , 777–779 (2002).

Previous studies of renal stone disease (RSD) in Thailand indicated abnormal urinary aggregator and inhibitor composition among farmers with excessive sweat loss. Our aim was to compare the proton MR spectra obtained from the kidneys of 32 proven cases of RSD (aged 38 to 65 yrs) with nine age-matched normal control subjects. We used the STEAM sequence with TE _ 15 ms and TR _ 2000 ms. The spectra at 3.25, 3.6 and 3.9 ppm were analyzed. The results showed a correlation between the three peaks (p _ 0.001), however, there was no significant difference between the RSD group and the normal control subjects. We therefore concluded that there was no overloading of these osmolytes among the renal stone patients.

1.1.7.4 Selvaraju, R., Thiruppathi, G., Raja, A., FT-IR spectral studies on certain human urinary stones in the patients of rural area, pages 260-265(2012) .

Fourier transform infrared spectroscopy (FT-IR) has been carried out to analyze the organic and inorganic constituent of human urinary stones. The FT-IR results indicate that stones have different composition, i.e., namely calcium oxalate, calcium phosphate, carbonate apatite and magnesium ammonium phosphate and uric acid. From the spectral and powder X-ray

diffraction pattern, the chemical constituents of urinary stones were identified. The quantitative estimations of calcium oxalate monohydrate (COM) 1620 cm^{-1} , calcium phosphate (apatite) 1037 cm^{-1} , magnesium ammonium phosphate (struvite) 1010 cm^{-1} , calcium carbonate 1460 cm^{-1} and uric acid 1441 cm^{-1} were calculated using particular peaks of FT-IR studies. The study reveals that calcium oxalate monohydrate and calcium phosphate type urinary stones were predominant whereas magnesium ammonium phosphate are in moderate level, and calcium carbonate and uric acid are in low. Calcium phosphate is found in all the stones and calcium oxalate monohydrate is found to be higher. Quantitative analyses of urinary stones show that calcium oxalate monohydrate (40%), apatite (30%), magnesium ammonium phosphate (23%) and uric acid (7%) are present in all the urinary stone samples.

1.1. 8 Aim of study

The present study was aimed to analyze the kidney stones (collected from 20-sudanese patients), and some dietary factors (black tea, tap-water and table salt).