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Define Ureteric Stones Composition by Infrared Spectroscopy and Study Associated Factors in South of Iraq

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Abstract
Infrared spectroscopic method (physical method) of stone analysis was used to study forty ureteric calculi that were extracted by different techniques or past spontaneously from patients with age range 2-63 years, 27male and 13 female, and overall sex ratio 2:1 .

We found the most common stones were pure calcium oxalate monohydrate 42.5% followed by pure uric acid stones 12.5% and ammonium acid urate 10% , pure stone constitute about 80% and mixed stones constitute about 20% with calcium oxalate monohydrate and uric acid (mixed stone) about 7.5% .

The risk of having specific type of stone was analyzed by selected predictor variables :- mixed type stone was significantly associated with past history of urolithiasis, gout with urate type of stone and young female with recurrent UTI with phosphate type of stone .

The success rate of stone retrieval by ureteroscopy and ESWL was found to be inversely related to:- UTI, past history of urolithiasis, mixed type of stone, stone size > 1.2 cm, phosphate variety of stones .

Stone distribution by age and sex was different according to the crystalline component of each type .

Chapter one
Introduction

History and prevalence of stone disease
Factors afflicted the causation of urolithiasis
Physical chemistry
Stone type
Analysis of urinary stones

History and prevalence of stone disease

Urinary stones have afflicted human kind antiquity, with the earliest recorded example being bladder and kidney stones detected in Egyptian mummies dated to 4800 Bc .
The prevalence of urinary tract stones is estimated to be 2-3% and likelihood that a man will develop stone disease by age 70 years is about one in eight, the recurrence rate without treatment for calcium oxalate renal stone 10% at one year, 35% at five years and 50% at ten years[1,2] .

Factors afflicted the causation of urolithiasis

Intrinsic factors
Heredity :
Genetic studies concluded that urinary stone is associated with a polygenic defect and partial pentrance. Several disorders that cause renal stone are hereditary. The genetic factors primarily are determinant in cystein stone formers and probably are significant in the formation of uric acid stones.

There is evidence of a polygenic inheritance of calcium oxalate stone in which two or more variables must be present to lead to urinary stones[3].

The capability of individuals to transport the intrinsic genetic tendencies toward urinary stone formation from area to area makes it likely that the major tendencies contributing to urinary stone resides in the individual[4] .
Age and Sex:
The maximum incidence of urinary stone appears to occur in the thirty to fifty years old and the incidence of urinary stone is more prevalent in males, about three males are afflicted for every female. These observations are generally confirmed by most studies of age and sex incidence of urinary stones[2].
Extrinsic Factors
1- Diet :
Urinary excretion of substances resulted from the dietary intake of various foods and fluids have a significant effect on the incidence of urinary stone[1]. Ingestion of excessive amount of purines, oxalate, calcium, phosphate and other compounds often result in excessive excretion of these components in urine[2]. A vegetarian diet is associated with childhood urinary stone, and habitual excessive ingestion of milk product in the form of cheese or ice cream will increase the incidence of stone formation[3] .

2- Water intake:
Two factors are involved in the relationship between water intake and urinary stones:
a. The volume of water taken compared to that lost by perspiration and respiration.
b. The elements content of the water supply of the region[2]. Increased water intake, which increase urinary output decrease the incidence of urinary stone in those patients who are predisposed to the disease[1].
The mineral or element content of water may also contribute to the causation of stone disease. Some state that excessive water hardness (e.g. sodium carbonate) causes a great incidence of stone disease. The presence or absence of certain trace elements in water has been implicated in the formation of urinary stone e.g. zinc is an inhibitor of calcium crystallization[5]. Low urinary level of zinc therefore may increase the tendency toward stone formation[6].
3-Geography:
The prevalence of urinary stone is higher in those who live on mountains, deserts and tropical areas[7].
Geography influences the incidence of urinary stone and the type of the stone that occurs within a given area, certain types of geography has an effect on temperature and humidity which influence the incidence of human urinary stone[1].
4- Climatic and seasonal factors:
There is a relationship between higher environmental temperature and higher incidence of urinary stone disease. A much higher incidence of urinary stone in the summer months is believed to be related to the effect of temperature, humidity and dehydration[3]. Higher temperature increase perspiration, which may result in concentrated urine, this promotes an increase in urinary crystallization[1].
5- Occupation:
The incidence of urinary stone is higher in administrative and sedentary personal than in manual workers[8]. The highest incidence was found in cocks and engineering room personal, this probably associated with a hoot environment[9].

Physical chemistry

Urinary stone do not occur unless crystals of the offending substance form in urine. For crystal to occur, the urine should be supersaturated with the salt in consideration. An increase in the urinary excretion of the chemicals that constitute the crystals results in an increase in the potential for crystallization[9].

Urine does not need to be continuously supersaturated for crystals to form or grow, intermittent super saturation, as is seen during periods of dehydration or after meals, is sufficient. Because urine is a complex solution, several factors affect the availability of ions required for crystallization. Thus the crystallizing potential for calcium oxalate is not related so much to the total concentration of calcium or oxalate in urine but it is related to the chemical activity of the ions in solution[4].

Compound such as citrate and phosphate can form complexes with calcium and other elements such as magnesium and sodium, effectively reducing the free ionic concentrations of each[10].

Urinary super saturation alone does not explain the formation of urinary stones. The urinary crystals can be seen in most individuals without formation of stones. Normal subject have inhibitors of crystal formation, growth and aggregation in their urine, which include: citrate, pyrophosphate, glycosaminoglycans, nephrocalcine and Tamm-Horsfall protein[11]. The free crystals which are normally formed within the kidney don't have the ability to grow to a large size enough to occlude a duct and form a stone in a free flowing urinary system. Crystal aggregation and retention within the kidney are prerequisite for urinary crystals to be converted to urinary calculi.

Crystal aggregation is enhanced in individuals who lack inhibitors of aggregation. The urinary glycoprotein nephrocalcine and Tamm-Horsfall proteins are potent inhibitors of crystal aggregation in the solution, where as citrate and magnesium are inhibitors of crystal growth[12].

Anatomical abnormalities such as medullary sponge kidney or ureteropelvic junction obstruction are increase stickiness of tubular epithelium and can predispose to increase crystal retention .

Although not proven, bacterial infections may promote calcium oxalate formation by increasing urinary matrix, which in turn promote adherence.

Finally, altered transport of calcium and oxalate by renal epithelial cells may result in intracellular or interstitial crystallization. These crystals are retained in the kidney and can become the nidus for stone formation[13].

Stone types

1- **Calcium oxalate stones** : is one of the most common types, comprising about 70% of all types especially in middle east[12]. It occurs in three crystalline forms:
* Calcium oxalate monohydrate (COM), (whewellite $CaC_2O_4.H_2O$)
* Calcium oxalate dihydrate (COD), (weddellite $CaC_2O_4.2H_2O$)
* Calcium oxalate trihydrate (COT), ($CaC_2O_4.3H_2O$)

Most calcium oxalate stones are composed of pure calcium oxalate, either alone or combined with calcium phosphate or urate.
Calcium stones may develop as result of excessive excretion of calcium (hypercalciuria), oxalate (hyperoxaluria), decrease urinary volume, hyperparathyroidism, urinary PH<6, congenital abnormalities, dietary habits, hot climate and presence or absence of inhibitors[14].
2- **Uric acid stones**: about 10-20% of urinary stones (C5H4N4O3), it crystallizes in monoclinic system. It affects middle age men more than young adults[15]. Persistent urinary acidity, decrease urinary volume, hyperuricoseuria, and increase protein level in the diet may be the main causes of uric acid stones. Especially in the industrialized countries and western world. Inborn errors of metabolism can cause uric acid stones in pediatric patients. Uric acid poorly soluble at PH< 5.5. Solubility increase with increasing urine alkalinity[16].
3- **Phosphate stones**: it comprises about 10-15 % of urinary stones and 30% of stones found in industrialized countries. It is also known as infection stone, five different phophates have been found in urinary stones: hydroxyappitate, struvate, brushite, whitlokite, and newbeyrite.
Appitate and struvate form the great bulk of the stones. Brushite occur in1-2% of stones. The other two occur rarely[14]. Phosphate stones are more common in females than males, it thought to be caused by infection in the urinary tract (by urea splitting bacteria) and in children it may occur because of anatomical defect[5]. The stone grow rapidly to a large size in the presence of an alkaline urine (PH>7) and urase-producing bacteria in the urine.
4- **Cystine stone**: (C6H12N2O4S2) are uncommon found in 1-3% in the whole world. It is crystallized in hexagonal system. Cystine stone occur as a result of cystineuria caused by inborn error of metabolism, so it may occur in early age in equal ratio in the male and female and it may occur in the age of 20-30 years[13]. Increasing urinary PH to >7.5 will increase cystine secretion[14].
5- **Xanthene stones**: (C5H4N4O2) are uncommon, it may found in children and adult of different ages[16].
6- **Silicate stones**: it is common in animals but very rare in human kind. It is thought that those patients who ingest large quantities[16] of magnesium trisilicate for a long time is likely to develop silicate stones[5].
7- **Mixed stones**: are those types of stone consisting of two or more of the above-mentioned types[14].

Crystalline components of urinary stones[14]

Component	Formula	Mineralogical name
Calcium oxalate monohydrate	CaC4O4.H2O	Whewellite
Calcium oxalate dihydrate	CaC2O4.2H2O	Weddelite
Magnesium ammonium phosphate hexahydrate	MgNH4PO4.6H2O	Struvite
Magnesium ammonium phosphate monohydrate	MgNH4PO4.H2O	Dittmarite
Calcium hydrogen phosphate dihydrate	CaHPO4.2H2O	Brushite
Carbonate-apatite	Ca10(PO4CO3)6(OH)8	Carbonate-apatite
Hydroxyl-apatite	Ca10(PO4)6(OH)2	Hydroxyl-apatite
Anhydrous tricalcium phosphate	Ca3(PO4)2	Whitlokite
Magnesium dibasic phosphate trihydrate	MgHPO4.3H2O	Newbeyrite
Uric acid	C5H4N4O3	Uric acid
Uric acid dihydrate	C5H4N4O3.2H2O	Uric acid dihydrate
Sodium acid urate	NaC5H3N4O3.H2O	Sodium acid urate
Ammonium acid urate	NH4C5H3N4O3.H2O	Ammonium acid urate
Cystine	C6H12N2O4S2	Cystine
Xanthene	C5H4N4O2	xanthene

Analysis of urinary stones

Urinary calculi are often small (< 5 mg) and can be composed of many different constituents. The highly variable composition has lead to the development of many different methods of calculi analysis.

In general the analytical methods can be divided into chemical and physical methods. Chemical methods are destructive and need several mg of sample, the smallest stones cannot be analyzed with chemical methods. Qualitative and semi quantitative chemical analysis methods are not accurate and can lead to clinically

significant errors[17].

Physical methods need fewer samples than chemical methods and can distinguish the different minerals in the stones. Thermal analysis can give quantities results but needs relatively much sample. Optical methods can analyze a few grains of stone but gives only qualitative results. Both methods cannot be used to analyze an unexpected stone. Best-suited methods for the analysis of calculi are X-ray diffractometry and infrared spectroscopy. X-ray diffractometry can detect crystalline minerals in low concentrations[18]. Infrared spectroscopy can detect both crystalline amorphous minerals. Both methods can be used for semi quantitative stone analysis and can analyzes less than 1 mg of stone sample. Both are the best methods to identify unexpected stone constituents[19].

There are three reasons of carrying out chemical and physical analysis for urolithiasis patients:

1- to diagnose the kind of urolithiasis process.
2- to control therapy and metaphylaxis.
3-to understand the genesis of urinary calculi.

Stone analysis by infrared spectroscopy

The principle of infrared spectroscopy is measurement of the wavelength of electromagnetic energy absorbed by the vibration of atoms in ions or molecules; this procedure is specific for atom groups. Molecular composition and crystal structure influence the absorption and resulting spectra are characteristic of each compound or mixture[33].

The infrared analysis is an easy and rapid procedure, able to identify all crystalline, amorphous or poorly crystalline components, mineral and organic molecules, and to distinguish between various crystalline phases of a given substance, moreover it is possible to quantify the relative proportion of the constituents in a mixed stone, the resulting spectra where identified by comparison with published references data and with IR tables (atlas)[34].

For determination of identity and purity of chemicals, infrared spectroscopy (IR) has played a special rule in research and technology for more than 25 years. This applies both to qualitative and quantitative analysis of substances or mixtures and for the structural analysis of chemical compounds. Infrared spectroscopy is one of the molecular spectroscopy techniques using oscillation spectroscopic method[20] . The polar bonds in polyatomic molecules such as $PO4^{-3}$ and oxalate absorb infrared (IR) light.

The fraction of infrared light absorbed depends on its wavelength, the nature of molecule, and the amount of molecule present in the infrared beam. Infrared spectra are recorded with infrared spectrophotometer and are represented as a percentage transmittance (%T) as a function of wave number $(\tilde{v})$ curve; percentage T is the relative amount of infrared light absorbed by the sample. $(\tilde{v})$ is the reciproque of the wavelength in Cm. Each molecule has its own specific infrared spectrum[21] . The infrared spectrum can change when the molecule is placed in a different crystalline environment. Infrared spectroscopy is used for the analysis of urinary calculi since the early 1950[22]. Identification of most calculi was done by mean of identification templates. These made identification of calculus constituents easy but a quantitative analysis was not possible. However, because the amount of infrared light absorbed by the sample depends on the amount of molecule present into the infrared beam, infrared spectroscopy can also be used for the quantitative analysis of urinary calculi [23]. The height of the absorption band proportional with the amount of absorbing molecules in the infrared beam. With the development of relatively inexpensive computers it became possible to replace the visual way of comparison by a computer assisted methods [26]. This approach makes it possible to compare many infrared spectra of unknown samples and standard reference spectra in few minutes.

Depending on the chemical bonding conditions, and also on the particular structure, every chemical molecule has a characteristic absorption spectrum in the infrared region, the "finger print of the molecule "[24,25].

1- Calcium oxalate stones:

* Whewellite: characteristic absorption is found at 655,781,883 and 984 cm^{-1}. The water of the hydration balance oscillation band is split into five single bands from 3058-3488 cm^{-1}.
* Weddelite: in contrast to whewellite, the water of hydration band at 3488 cm^{-1} is wide and not split. The absorption at 608 and 910 cm^{-1} are also characteristic.

2- Urate stones:

* Uric acid: the infrared spectra of uric acid and its salts have many bands. Intense absorption can be easily recognized even in mixtures. The band grouping from 400-800 cm^{-1} is especially important; other characteristic absorption is present at 1591, 1675, and 2825 and 3010 cm^{-1}.
* Ammonium acid urate: the band at 598 cm^{-1} clearly identifies ammonium urate from uric acid, in addition the band grouping between 1200 and 1600 cm^{-1} is characteristic.

3- Phosphate stones:

* Struvite: can be identified by the typical bands at 571,760 and 1004 cm^{-1}.

* Brushite: this acid calcium phosphate can be distinguished from other phosphate by the multiple splitting of phosphate band between 800 and 1200 cm^{-1}.
4- Cystine stone: characteristic bands are present at 400-500 cm^{-1}. the band grouping between 1200 and 1600 cm^{-1} is important for identification in mixture.
5- Mixed stones: identified by various combinations of two or more of the above-mentioned spectra[24,25].

Chapter two:
Aim of study.
patients and method.

Aim of the study:
* To study the chemical composition of different types of ureteric stones using infrared spectroscopic analytic method for ureteric stones extracted by an ultrasonic ureteroscopic lithotripsy, ESWL, ureterolithotomy, and spontaneously passed stones.
* To delineated the variable risk factors of having specific types of stones.
* To assess the effect of specific types of stones on the success of minimally invasive procedures of stone extraction.

Patient and methods
1- Samples collection and preparation:
During the period from May 2016 to February 2017, fragments from 40 ureteric stones were collected from patients treated with ultrasonic ureteroscopic lithotripsy for ureteric stones, ESWL, ureterolithotomy, and patients with spontaneous passage of ureteric stones.
2- Samples preparation for infrared spectroscopy:
Each stone sample was washed with distilled water, dried in room temperature then each sample was ground into fine powder and mixed with 100 mg of potassium bromide (KBr) powder in an agate mortar, this mixture was then pressed with a compression machine to form a transparent pellet (13 mm)in diameter. The pellet was mounted in a holder and placed in infrared beam of the spectrometer. The infrared analysis of the studied samples was done by SP 3-300 infrared spectrophotometer in Geology department in the college of sciences. The absorption spectrum were compared with standard published reference spectra to identify the components of the samples.
3- Patients were made to answer a standard questionnaire addressing their symptomatology, risk factors and associated conditions.

Chapter three:
Results
Discussion
Conclusion

Results
Description of study samples:
There were forty ureteric calculi obtained from 27 male (67.5%) and 13 (32.5%) females giving a male to female ratio 2:1, their ranged between 1-63 years (mean 32 years) (table 1). 7 stones were upper ureteric (57.5 %),10 stones were midureteric (25%), 23 stones were lower ureteric (57.5). 17 stones (42.5%) were retrieved by ultrasonic ureteroscopic lithotripsy, 9 stones (22.5) were retrieved by ESWL and 12 stones (30%) retrieved by ureterolithotomy, two stones (5%) were obtained from patients with spontaneous passage of ureteric calculi (table 2). 80% of patient presented with ureteric colic, 70.5% presented with hematuria (macroscopic and microscopic) and 2.5% ureteric stones were detected incidentally.

62.5% of patients have no past history of urolithiasis whereas 27% have past history of renal stone, 7.5% with history of ureteric stones and 2.5% of vesical stones. 30% of the patients have family history of urolithiasis and 35% of patients have a positive ureteric culture (E.coli 42.5%, proteus species 35.7%, staph. aureus 21.4%) (table 3). 5% of patients have a history of gout, 12.5% were uremic, and 2.5% of patients have history of renal tubular acidosis and 10% 0f patients have history of pyelonephritis (table 4).
The chemical composition of stones as analyzed by infrared spectroscopy:
The most common chemical composition of the stones as analyzed by infrared spectroscopy was calcium oxalate monohydrate (42.5%) of the total number of stones while uric acid and ammonium acid urate stones represented 22.5% of the total number, various other chemical builds were detected in the rest of the stones analyzed shown in decreasing order of frequency in the table 5 and figure 1.

The mineralogical components of the whole stones sample are shown in table 6 and figure 2.

The risk of having mixed stones by selected predictor variables:

A mixed type of stones was more frequently obtained from subjects with a positive past history of urolithiasis (40%) compared to those with negative history (8%). The risk of having a mixed type of stone on subjects with past history of urolithiasis is 7.7 times higher than those with negative history. The calculated OR was statically significant P value =0.04.

The rate of mixed type stones was obviously higher in females (38.5%) than males (11.1%). Female gender increases the risk of having mixed stones by five times compared to males (OR =5) P value =0.09. Also for those with positive family history of urolithiasis (33.3%) than negative history (14.3%) this category has risk of having mixed stone by 3.3 (OR =3.3) P value =0.21. (table 7)

The risk of having urate type of stone by selected predictor variables:

Although associations observed in this category of stones with patients having gout (100%), past history of urolithiasis increased risk (40%) than negative history (16%) (OR =3.5) P value =0.14 also positive urine culture increase risk (35.7%) than negative urine culture (19.2%) (OR =2.3) P value =0.28.(table 8)

The risk of having phosphate type of stones by selective predictor variables:

The rate of phosphate stone was obviously higher in females (30.8%) than males (7.4) (OR =5.6), P value =0.08, and those with positive urine culture (documented UTI) have risk of having phosphate type of stone by 4.8 for positive culture (28.6%) than those with negative urine culture (7.7%) (OR =4,8) P value =0.16 . Positive family history of phosphate type of stone increased risk of having this type by 2.8 (OR =2.8) P value =0.34 . (table 9)

The risk of having oxalate type of stone by selected predictor variables:

The following associations were observed in this category of stones with male gender (77.8%) than female (61.5%) (OR =2.2) P value =0.45, and with patient with negative urine culture (80.8%) than those with positive urine culture (57.1) (OR =3.1) P value =0.15 also with those with negative past history of urolithiasis (84%) than those with positive history (58.3%) (OR =2.6) P value =0.25 (table 10)

The success rate of stone retrieval by ureteroscopy / ESWL method by selected independent (explanatory variables):

The following associations were observed and may suggest increasing success of stone retrieval ureteroscopy / ESWL (in opposite to ureterolithotomy):

Negative urine culture increase the chance of success (75%) than positive urine culture (57.1%) (OR =2.3) P value =0.3 . also positive past history of urolithiasis decrease risk of success (60%) for positive history and (73.9%) for negative history (OR= 2) P value =0.23.

Phosphate type of stones was observed to decrease success rate 933.3%) than other types (75%) (OR =5.9) P value =0.07. (table 11,12)

stone distribution by age and gender was found to be different with different crystalline components of urinary stones. (table 13)

Tables

Table 1: Frequency distribution of the study sample by sociodemographic variables.

	N	%
Age in years		
1-10	7	17.5
11-20	4	10
21-30	8	20
31-40	14	35
41-50	4	10
>50	3	7.5
Gender		
Female	13	32.5
Male	27	67.5
Total	40	100

Table 2: Frequency distribution of the study sample by stone site and stone retrieval method.

	N	%
Stone site		
Upper ureteral	7	17.5
Mid-ureteral	10	25
Lower ureteral	23	57.5
Stone retrieval method		
Ureteroscopy	17	42.5
ESWL	9	22.5
Ureterolithotomy	12	30
Spontaneous passage	2	5
Total	40	100

Table 3: Frequency distribution of positive urine culture by type of bacteria isolated.

	N	%
Positive isolates of urine culture		
E.coli	6	42.5
Staph. aureus	3	21.4
Proteus spp	5	35.7
Total	14	100

Table 4: frequency distribution of the study sample by selected clinical variables.

	N	%
Chief complaint		
Pain	32	80
Hematuria	7	17.5
Incidental	1	2.5
Observed associated conditions		
None	28	70
Gout	2	5
Uremia	5	12.5
Pyelonephritis	4	10
RTA (renal tubular acidosis)	1	2.5
Past history of urolithiasis		
Negative	25	62.5
Renal	11	27.5
Ureteral	3	7.5
Vesical	1	2.5
Positive urine culture		
Negative	26	65
Positive	14	35
Family history of urolithiasis		
Negative	28	70
Positive	12	30
Total	40	100

Table 5: Frequency distribution of the study sample by stone chemical type analyzed by infrared-spectroscopy.

	N	%
Stone chemical type analyzed by infrared-spectroscopy		
Pure		
COM(calcium oxalate monohydrate)	17	42.5
UA(uric acid) anhydrous	5	12.5
Ammonium acid urate	4	10
COD(calcium oxalate dihydrate)	3	7.5
Struvite(ammonium magnesium phosphate Hexahydrate)	2	5
Brushite (calcium phosphate dihydrate)	1	2.5
Mixed		
(COM+UA)	3	7.5
(COM+COD)	2	5
(COM+Brushite)	1	2.5
(COD+Brushite)	1	2.5
(Struvite+UA)	1	2.5
Type of stone composition		
Pure	32	80
Mixed	8	20
Total	40	100

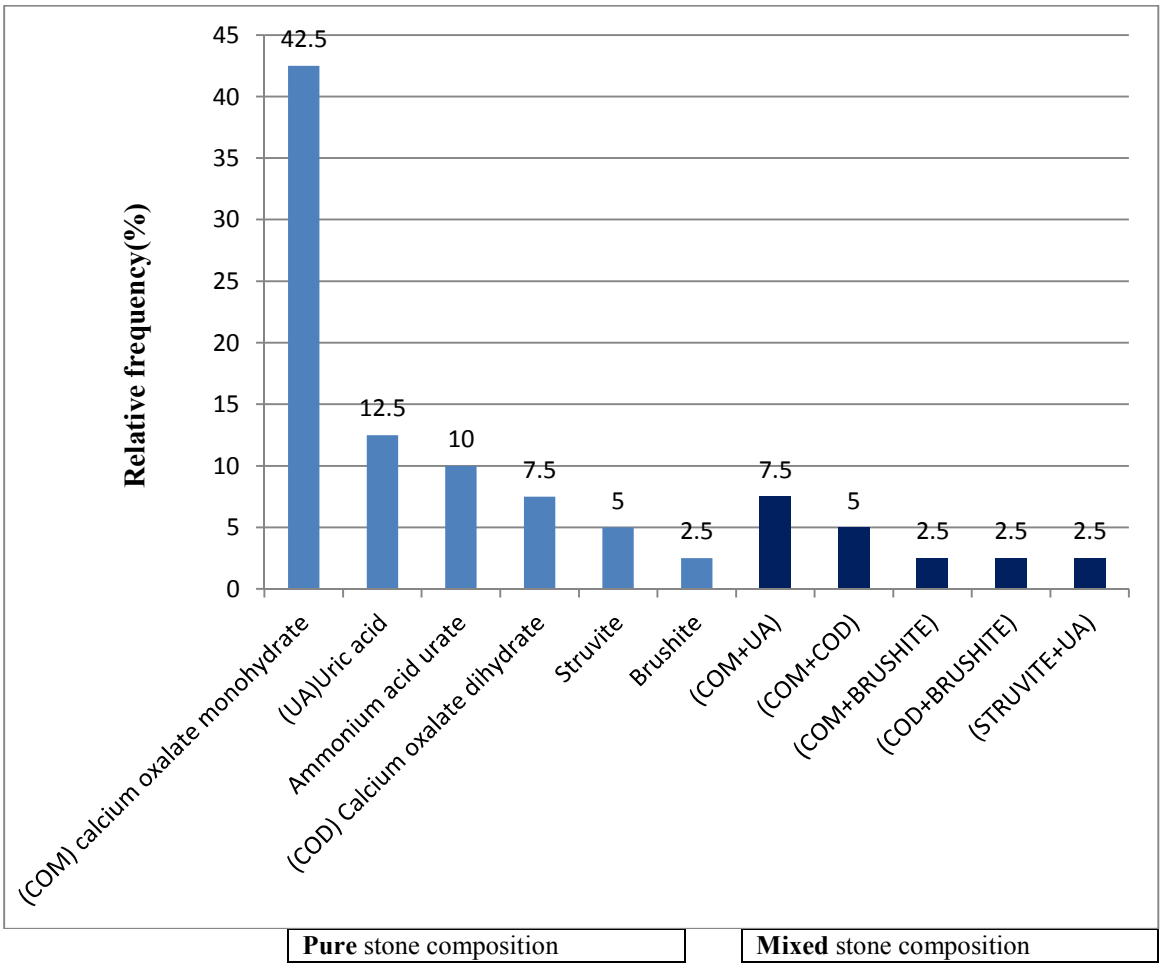

Figure 1 :Bar chart showing the relative frequency of different types of stone analyzed by infrared-spectroscopy

Table 6: The relative frequency of main mineral components of analyzed renal stones:

N=40	N	%
Main mineral components of renal stones		
Anions		
Oxalate $(C2O4)^{-2}$	29	72.5
Urate $(C5H3N4O3)^{-1}$	10	25
Phosphate $(PO4)^{-3}$	6	15
Cations		
Calcium $(Ca)^{+2}$	28	70
Ammonium $(NH4)^{+1}$	7	17.5
Magnesium $(mg)^{+2}$	3	7.5

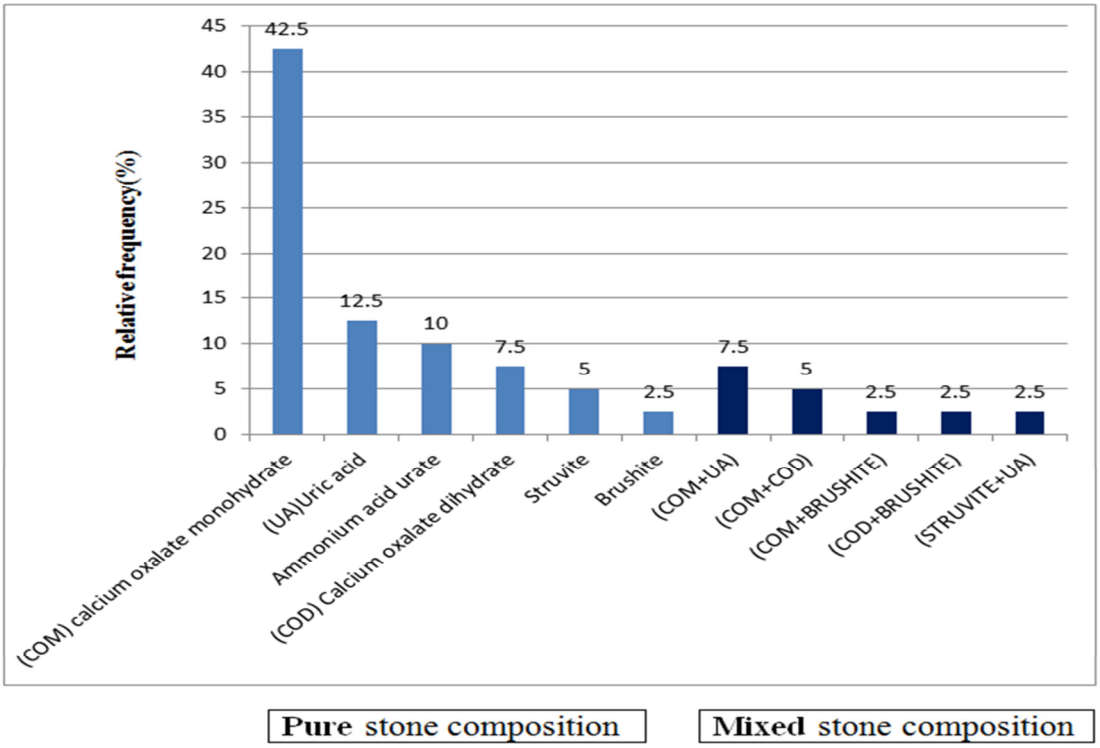

Figure 2 :Bar chart showing the relative frequency of main mineral components of analyzed renal stones.

Table 7: The risk of having mixed stone by selected predictor variables.

	Total N	**Mixed chemical composition** N	%	OR
Age				
1-30	19	3	15.8	Ref
> 3	21	5	23.8	1.7
P value = 0.7[NS]				
Gender				
Female	13	5	38.5	5
Male	27	3	11.1	Ref
P value = 0.09[NS]				
Chief compliant				
Pain	32	6	18.8	1.4
Hematuria	7	1	14.3	Ref
P value = 1[NS]				
Observed association condition				
Gout	2	0	0	
Uremia	5	2	40	
Pyelonephritis	4	0	0	
RTA(renal tubular acidosis)	1	0	0	
P value = 0.25[NS]				
Urine culture				
Negative	26	6	23.1	1.8
Positive	14	2	14.3	Ref
P value = 0.69[NS]				
Family history of urolithiasis				
Negative	28	4	14.3	Ref
Positive	12	4	33.3	3.3
P value = 0.21[NS]				
Stone site				
Upper ureteral	7	1	14.3	
Mid- ureteral	10	4	40	
Lower ureteral	23	3	13	
P value = 0.22[NS]				
Past history of urolithiasis				
Negative	25	2	8	Ref
Positive	15	6	40	7.7
P value = 0.04[NS]				

Table 8: The risk of having urate type of stones by selected predictor variables

	Total	**Urate salts**		
	N	N	%	OR
Age				
1-30	19	5	26.3	1.1
> 3	21	5	23.8	Ref
P value = 1 *[NS]*				
Gender				
Female	13	4	30.8	1.6
Male	27	6	22.2	Ref
P value = 0.7 *[NS]*				
Chief compliant				
Pain	32	8	25	Ref
Hematuria	7	2	28.6	1.2
P value = 1 *[NS]*				
Observed association condition				
Gout	2	2	100	
Uremia	5	2	40	
Pyelonephritis	4	0	0	
RTA(renal tubular acidosis)	1	0	0	
P value = 0.04 *[NS]*				
Urine culture				
Negative	26	5	19.2	Ref
Positive	14	5	35.7	2.3
P value = 0.28 *[NS]*				
Family history of urolithiasis				
Negative	28	6	21.4	Ref
Positive	12	4	33.3	1.8
P value = 0.45 *[NS]*				
Stone site				
Upper ureteral	7	4	57.1	
Mid- ureteral	10	3	30	
Lower ureteral	23	3	13	
P value = 0.07 *[NS]*				
Past history of urolithiasis				
Negative	25	4	16	Ref
Positive	15	6	40	3.5
P value = 0.14 *[NS]*				

Table 9: The risk of having phosphate type of stones by selected predictor variables

	Total	**Phosphate salts**		
	N	N	%	OR
Age				
1-30	19	3	15.8	1.1
> 3	21	3	14.3	Ref
P value = 0.1 *[NS]*				
Gender				
Female	13	4	30.8	5.6
Male	27	2	7.4	Ref
P value = 0.08 *[NS]*				
Chief compliant				
Pain	32	6	18.0	
Hematuria	7	0	0	
P value = 0.57 *[NS]*				
Observed association condition				
Gout	2	0	0	
Uremia	5	1	20	
Pyelonephritis	4	1	25	
RTA(renal tubular acidosis)	1	1	100	
P value = 0.26 *[NS]*				
Urine culture				
Negative	26	2	7.7	Ref
Positive	14	4	28.6	4.8
P value = 0.16 *[NS]*				
Family history of urolithiasis				
Negative	28	3	10.7	Ref
Positive	12	3	25	2.8
P value = 0.34 *[NS]*				
Stone site				
Upper ureteral	7	2	28.6	
Mid- ureteral	10	2	20	
Lower ureteral	23	2	8.7	
P value = 4 *[NS]*				
Past history of urolithiasis				
Negative	25	3	12	Ref
Positive	15	3	20	1.8
P value = 0.65 *[NS]*				

Table 10: The risk of having calcium oxalate type of stones by selected predictor variables

	Total	**Oxalate salts**		
	N	N	%	OR
Age				
1-30	19	13	68.4	Ref
> 3	21	16	76.2	1.8
P value = 0.73[NS]				
Gender				
Female	13	8	61.5	Ref
Male	27	21	77.8	2.2
P value = 0.45[NS]				
Chief compliant				
Pain	32	23	71.9	1
Hematuria	7	5	71.4	Ref
P value = 0.1[NS]				
Observed association condition				
Gout	2	0	0	
Uremia	5	3	60	
Pyelonephritis	4	4	100	
RTA(renal tubular acidosis)	1	0	0	
P value = 0.02[NS]				
Urine culture				
Negative	26	21	80.8	3.1
Positive	14	8	57.1	Ref
P value = 0.15[NS]				
Family history of urolithiasis				
Negative	28	22	78.6	2.6
Positive	12	7	58.3	Ref
P value = 0.25[NS]				
Stone site				
Upper ureteral	7	3	42.9	
Mid- ureteral	10	7	70	
Lower ureteral	23	19	82.6	
P value = 0.13[NS]				
Past history of urolithiasis				
Negative	25	21	84	4.5
Positive	15	8	53.3	Ref
P value = 0.07[NS]				

Table 11: The success rate of stone retrieval by ureteroscopy/ESWL method by selected independent (explanatory variable).

	Total N	**Successful stone retrieval by URS/ESWL method** N	%	OR
Age				
1-30	19	13	72.2	1.4
> 3	21	13	65	Ref
P value = 0.63 *[NSJ]*				
Gender				
Female	13	9	69.2	1.1
Male	27	17	68	Ref
P value = 1 *[NSJ]*				
Urine culture				
Negative	26	18	75	2.3
Positive	14	8	57.1	Ref
P value = 0.3 *[NSJ]*				
Family history of urolithiasis				
Negative	28	19	70.4	1.4
Positive	12	7	63.7	Ref
P value = 0.71 *[NSJ]*				
Stone site				
Upper ureteral	7	5	71.4	
Mid- ureteral	10	7	70	
Lower ureteral	23	14	66.7	
P value = 0.97 *[NSJ]*				
Past history of urolithiasis				
Negative	25	17	73.9	2.0
Positive	15	9	60	Ref
P value = 0.48 *[NSJ]*				

Table 12: The success rate of stone retrieval by ureteroscopy/ESWL method by anionic chemical composition of stones.

	Total **N**	**Successful stone retrieval by ureteroscopy/ESWL method** N	%	OR
Mixed chemical composition				
Pure	30	22	73.3	2.8
Mixed	8	4	50	Ref
P value = 0.23 *[NSJ]*				
Oxalate				
Negative	10	7	70	1.1
Positive	18	19	67.9	Ref
P value = 1 *[NSJ]*				
Urate				
Negative	29	19	65.5	Ref
Positive	9	7	77.8	1.8
P value =0.69 *[NSJ]*				
Phosphate				
Negative	32	24	75	5.9
Positive	6	2	33.3	Ref
P value =0.07 *[NSJ]*				
Stone size				
< 1.2 cm	22	18	82.4	2.25
> 1.2 cm	18	8	44.2	Ref
P value =0.08 *[NSJ]*				

Table 13: The relative frequency of different chemical stone types by age and gender.

	Age in years			GENDER		
	1-30	> 30	P value	Female	Male	P value
Pure						
COM	6 31.6	11 52.4	0.22[NS]	2 15.4	15 55.6	0.02[NS]
COD	2 10.5	1 4.8	0.59[NS]	1 7.7	2 7.4	1[NS]
UA	2 10.5	3 14.3	1[NS]	2 15.4	3 11.1	1[NS]
Ammonium acid urate	3 15.8	1 4.8	0.33[NS]	1 7.7	3 11.1	1[NS]
Struvite	2 10.5	0 0	0.22[NS]	1 7.7	1 3.7	1[NS]
Brushite	1 5.3	0 0	0.48[NS]	1 7.7	0 0	0.33[NS]
Mixed						
COM+COD	2 10.5	0 0	0.22[NS]	1 7.7	1 3.7	1[NS]
COM+UA	1 5.3	2 9.5	1[NS]	2 15.4	1 3.7	0.24[NS]
COM+Brushite	0 0	1 4.8	4.8[NS]	1 7.7	0 0	0.33[NS]
COD+Brushite	0 0	1 4.8	4.8[NS]	0 0	1 3.7	1[NS]
Struvite+UA	0 0	1 4.8	1[NS]	1 7.7	0 0	0.33[NS]
Total	19 100	21 100		13 100	27 100	

COM= Calcium Oxalate Monohydrate
UA= Uric Acid (anhydrous)
COD= Calcium Oxalate Dihydrate
Struvite= Ammonium Magnesium Dihydrate
Brushite= Calcium Phosphate Dihydrate

Statistical analysis:

Data were translated into a computerized database structure. An expert statistical advice was sought for.

Frequency distributions for selected variables were done first. To measure the strength of association between 2 categorical variables, such as a positive family history of renal stone and having a urate type stone, the odds ratio (OR) was used. The OR equals the ratio of the odds of having a positive family history versus lacking it among subjects with urate stone to the similar odds among those with stones not containing urate in their structure, table 2.1. The statistical significance of the measure OR is assessed by a special X^2 formula.

		Urate stone	
		+	-
Family history of urolithiasis	+	**A**	**B**
	-	**C**	**D**

$$OR = \frac{\frac{A}{B}}{\frac{C}{D}} = \frac{AD}{BC}$$

The relative risk is the real measure of association between exposure to certain factor and having the disease or outcome, but it needs a cohort study, in which the exposure status is determined first and the study subjects are followed for a long period of time to assess the development of the disease of interest. The present study is an analytic cross-sectional study, in which the calculated OR is the best estimate for the real measure of risk (RR), which can be calculated in cohort studies only.

The statistical significance of association between 2 categorical variables was assessed by Chi-square test or by Fisher's exact significance if the criteria for a valid Chi-square test were not met. An estimate was considered statistically significant if its P value was less than an α level of significance of 0.05.

Discussion:

Infrared spectroscopy was used as analytic technique in our study because of its availability, accuracy, and ability to determine the different crystalline components of urinary stones[33].

In agreement with large series published [27,28,29,30] , calcium oxalate was the most frequent component of urinary calculi (67%), pure calcium oxalate stones constitute the majority with (50%) of the total sample, calcium oxalate monohydrate was found to constitute about (42.5%) of the total stone components and more than (85.18%) of calcium oxalate stones.

Comparing our data with those published expressed as frequencies of main components we found similar result but some discrepancies. Some authors describe the predominance of calcium oxalate dihydrate calculi over calcium oxalate monohydrate [27] but this was reversed in our study.

Studies concerning ureteric stone composition in Iraq were came across as a moiety of a more wide projects concerning with urinary stones in general [34,35] . Alnaizi, N.A. described the most common chemical composition of ureteric stones that passed after ESWL and analyzed by infrared spectroscopy is the mixed type in 70% of cases[35] , Al-Shammary, E.J.described the common type of ureteric stones in pediatric age group in Iraq (as part of the study) was the urate type [34] .

Calcium oxalate lithiasis was preponderant in both sexes. The proportion of calcium oxalate monohydrate lithiasis was slightly higher in men than in women.

Urate stones constitute the second predominant stone category in our patients (22.5%0 for the two main components of urate stones (uric acid and ammonium acid urate), although uric acid stones have some male predominance in our study , the ammonium acid urate stone had more male predominance and occur at younger age than uric acid stones. Ammonium acid urate calculi usually occur in children with UTI and decrease fluid intake in children in developing countries [39] .(Klhon et al,1986). the frequencies of urate stones were similar to those of other series [28,29] .

Phosphate stones were shown to have a direct relationship with female with recurrent urinary tract infection (induced by urea splitting bacteria)[38] .

Mixed stones were found to constitute about 20% of our sample with predominance of calcium oxalate component. The combination of calcium oxalate monohydrate and uric acid was observed in 7.5% of our sample.

Cystein stones were not found in our sample because of the rarity of these stones and the limited size of our sample.

In our study 35% of patients had positive urine culture (documented UTI), E.coli was isolated from 42.9% of those patients followed by proteus spp. (35.7%). In one study (Holm-Gren et al1989),371 0f 1325 patients hospitalized with stone disease has positive culture at sometime during follow up, surprisingly E.coli was the most common microorganism identified on urine culture, the prevalence being higher than that of proteus spp. , and the patient with E.coli infections 15% had Struvite stone[36] .

Dutoit and colleagues 1989 demonstrate that E.coli decrease urokinase and increase sialidase activity, this may lead to production of urinary matrix substance, increase crystal adherence to the renal epithelium[37] .

We noticed a relatively low frequency of infections lithiasis (Struvite) 7.5% compared with the early series. This probably due , first, to the earlier detection of urinary infection and secondly the greater attention paid to their treatment in recent years. This is confirmed by the progressive decrease in the frequency of infection stones, as shown in the chronological data presented in our study as did [27].

The sex ratio (men: women) changed with the crystalline composition of calculi. In agreement with Leusmann andKoide, the overall sex ratio in our study was (2:1)[22,27,32].

The success rate of stone retrieval by ureteroscopy and ESWL[31] :

The introduction of new techniques gave extra opportunities to treat ureteric stones. Although 5% of these stones passed spontaneously, methods other than open surgery used , and we evaluate the factors affecting the success rate of stone retrieval by these methods and found to be inversely related to urinary tract infection, past history of urolithiasis, mixed type of stones, stone size >1.2 cm, and phosphate variety of stones [31] (table 11,12).

Bacterial infection causes alkalinity of urine, increase crystal adherence (urea splitting organisms), increase production o urinary matrix substances and increase crystal adherence to the epithelium(E.coli).

The stone size and composition of the stone group of this study have positive correlation with success rate, the shock waves normally tend travel in a straight direct path unless they are made to deviate by scattering centers, large stone size lead to prolong propagation path which may result in attenuated waves, also increase stone size lead to increase stone density which is inversely related to success rate (correlation between the density of the stone with number of shock waves)[35] .

Mixed stones occur when a crystal has a pattern of other crystal from other types (Epitaxy), a slight change in crystal disorientation is associated with an intersecting sub-boundary and gives larger size of the stone, which tend to loss the shock wave energy[35] .

Phosphate stones usually present as mixed stones (Ca-Ph, MAP..) and associated with UTI and to be present with large size (Struvite calculi account for majority of staghorne calculi and usually harbor infecting bacteria within their intersects)[38] . Patient with history of recurrent stones tend to have large and mixed type of stones[38].

During the analysis of risk factors of having specific type of stones we found the direct relationships of past history of urolithiasis with mixed stone and history of gout with urate type of stone[40], young female with recurrent UTI with phosphate stones (table 7,8,8,10) and these findings correlate with other studies[38,40,41,42].

Ureteric stones distribution by age and gender (table 13) was found to be variable according to the different crystalline components of each type stones which was comparable with the previously published series[32].

Conclusion

- Infrared spectroscopy as physical analytic method for urinary calculi composition for identification of the monocrystalline components of urinary calculi may be the preferable method for study of the composition of stones because it is reliable, simple, quick, and cheep.
- The pure and mixed calcium oxalate monohydrate stones are the most common ureteric stone observed in our patients.
- Stone types were noticed to have some epidemiological variables that can be prevented.
- Success of a particular stone destruction method may be related to the type of the stone.

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