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DETERMINATION OF URINARY STONES CHEMICAL COMPOSITION BY COMPUTED TOMOGRAPHY DENSITY

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ABSTRACT
Objectives: To assess the role of Computed Tomography (CT) in identify the chemical composition of urinary stone according to Hounsfield Units (HU) value and to assess the accuracy of CT in determination the chemical composition of urinary stone in comparison with chemical stone analysis and urine examination.
Background: Renal stone is one of the most common causes of acute abdomen pain. There are many types of renal stones depending on stone chemical components those including calcium oxalate stone, calcium phosphate, struvite stone, uric acid stone and cystine stone. CT are more valuable diagnostic imaging modalities in describing and evaluating the renal stone site, size and density in HU.
Patients and methods: A total of 80 patients were examined, their age was ranged from 20 to 79 year. All patients were examined with Computerized Tomography of Kidney, Ureter and Bladder (CT KUB) examinations to identify renal stone density. Laboratory tests of urine to identify type of stone depended on PH level test and crystals appearance in microscopic urine examination.
Results: According to the stone densities those determined by CT, the renal stones were divided into three groups, the first group; low density such uric acid stone their densities range 200-450 HU, the second group: medium density such cystine stone, struvite stone and mixed (calcium oxalate and uric acid) stone their densities range 450-600 HU and the third group: high density such calcium stone (oxalate or phosphate) their densities range 600-1700 HU.
According to PH of urine analysis, the renal stones were divided into two groups, PH of uric acid stones and cystine stone was less than 6, PH of calcium oxalate stones, struvite stones and calcium phosphate stones was more than 6.
Conclusion: All urinary calculi examined were clearly visible on CT regardless of chemical type. We found the chemical composition of urinary calculi can be accurately predicted by CT using the HU parameters. HU parameter in computerized tomography can distinguish uric acid stones from calcium oxalate stones with high accuracy.
Keywords: CT, HU, PH, renal stone density

INTRODUCTION
Renal calculi formation is seen as a common worldwide clinical problem; basically the formation of calculi occurs in kidney (nephrolithiasis), ureter (ureterolithiasis) and urinary bladder (cystolithiasis)[1]. Urolithiasis is the process of stone formation in different portions of the urinary tract, including the kidneys, ureter, bladder, and/or urethra. It represents a worldwide

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problem associated with high healthcare costs due to surgical interventions for its resolution and subsequent medical care [2]. Many factors contribute to the etiopathogenesis of urolithiasis: diet (increased animal proteins and refined sugar and salt consumption), sex (the disease is more common among men than among woman), age, low fluid intake, genetic factors, and geographic factors[3]. Similarly, the association between metabolic syndrome (which includes obesity, hypertension, high triglyceride levels, and diabetes) and kidney stone disease is well established[4]. Dietary modification is key to prevent stone formation and recurrence. Strict control of calcium, oxalate, fructose, salt and protein consumption as well as the necessary fluid intake to produce at least 2–2.5 l of urine per day is vital [5]. In general, urinary stones may contain various combinations of chemicals. The most typical stones contain calcium in combination with either oxalate or phosphate. Much less common are the uric acid stones and the rare cystine stones. The main cause of calcium oxalate stone is dietary oxalate contributes to about half of the urinary oxalate. Spinach, rhubarb, beets, chocolate, nuts, tea, wheat bran, strawberries, and soya foods are known to increase urinary oxalate concentrations. Also, vitamin C supplementation may increase urinary oxalate excretion[6]. Calcium oxalate stones usually have a dark brown color, the surface is often mulberry like and the stones are very hard[7]. However, as a high urinary pH will encourage calcium phosphate stone formation, increased urinary pH decreases the solubility of calcium phosphate, thereby increasing the risk of nephrocalcinosis and kidney stones [8]. Phosphate is less soluble at alkaline versus acidic pH, so phosphate precipitates on to the insoluble ammonium products to form struvite stones [1], It has a white or gray color, the surface is mostly smooth and the consistency ranges from solid to slackened [7]. Excessive consumption of meat protein might increase the risk of developing uric acid stones because meat causes the over acidification of urine [6], A low urine pH of ≤5.5 leads to a higher concentration of insoluble uric acid crystals [9]. The color of the uric acid stones varies from light yellow to red-yellow, their surfaces are mostly very smooth [7]. Struvite stones are most commonly due to urinary tract infections caused by urease producing bacteria and require alkaline urine to form, in previous reports, females produced the largest number of struvite stone [10], the color is mostly white to light gray[7]. Cystine stones are due to an intrinsic metabolic defect causing the failure of the renal tubules to reabsorb cystine, lysine, ornithine, and arginine [11], Stones of cystine have yellow color, the consistency is very solid [7]. Non-contrast computed tomography (NCCT) has the highest sensitivity and specificity to detect stones and is the most accurate imaging modality to measure their size, but also to be useful for estimating the mineral composition of the stones[12]. Although NCCT is the standard investigation for diagnosing acute flank pain, and is also good for detecting stone location, size, and density measurement in addition to predicting stone composition by using the CT number (HU) [13]. CT imaging can also provide information regarding the composition of stones. Attenuation describes the density of objects encountered by photons passing from the radiation source to the detector. The Hounsfield units of a stone can indicate its type; as different stone compositions absorb differing amounts of radiation [14]. Hounsfield units, a parameter generated from standard CT, are related to the density of the stone or structure of interest. Recent studies suggested that HU and their variants are useful for predicting the composition of stones. However, they were insufficient for certain types of stone; the use of urinary parameters improved the accuracy in such cases[15]. The phosphate calculi among the densest 1700 HU on CT, the relatively low attenuation < 450 HU of uric acid calculi on CT [16]. All patients should undergo a simple urinalysis. Urine pH plays a critical role in stone composition, acidic urine promotes UA, calcium oxalate and cystine stones, whereas alkaline urine promotes calcium

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phosphate and struvite stones [17]. The urine sediment should be analyzed with a microscopic examination. In some cases, crystals identified by microscopy can predict the composition of stones formed by the patient. The presence of hexagonal crystals is pathognomonic for Cystinuria. Rectangular “coffin-lid” crystals are commonly encountered in patients with struvite calculi. Calcium oxalate stone formers may demonstrate tetrahedral “envelope” crystals. Calcium phosphate stone are colorless and may appear as star-like or needle-like crystals. Barrel, plate-like crystals are indicate presence uric acid stone [18].

PATIENTS AND METHODS

The data used in this study was collected from Institute of X-Ray at medical city/Baghdad. The study included 80 patients with clinical and ultra-sonographic diagnosis of urinary tract stone. Patients ages range were (20 years- 79 years) with mean age (47 years), the males were 53 patients and females were 27 patients, patients were referred to urine analysis and Computerized Tomography of Kidney, Ureter and Bladder (CT KUB) examinations, during period of five months starting from November 2020 to March 2021. NCCT was performed with a multidetector helical scanner Aquilion 64, Toshiba, slice thickness 5 mm, dose 120 KV and 40- 200 mAs.

CT KUB TECHNIQUE:

a- Preparation of the Patient: Take off some or all of the clothing and wear a hospital gown, remove metal objects.

b- Patient Position: The patients with urolithiasis are lying supine position on a scan table that slides into a large, circular opening of the scanning machine. Pillows and straps may be used to prevent movement during the procedure, with arms placed above the head and the head to be first on the examination table, explaining to patient to stay still and avoiding movements. Topogram is taken first in AP to map the exact distance of the CT volume.

C - Stone Protocol: The patient with urolithiasis is placed into the ionizing radiation field of the CT-unit and a Technician will be doing the examination whilst working in the computer outer of the room. The coverage area for a stone protocol CT extends from the upper pole of both kidneys to the base of the urinary bladder, the actual CT- Stone procedure exam takes the time at about less than 60 seconds.

RESULTS

This study including 80 patients 53 males (66.25%) and 27 females (33.75%) in Institute of X-Ray at medical city/Baghdad. The age of patients ranges from 20 – 79 years old and the Mean ± SD age of study sample was 47.93±13.16.

Table 1: Distribution of studied sample according to, Age groups, Gender.

		No.	%
Gender	Males	53	66.25
	Females	27	33.75
	Total	80	100.00
.	20-29	6	7.50
	30-39	10	12.50
	40-49	31	38.75
	50-59	20	25.00

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Age groups	60-69	10	12.50
	70-79	3	3.75
	Total	80	100.00
	Mean ±SD=47.93±13.16		

Highest percentage (38.75%) in age group 40-49 years while the low percentage (3.75%) in age group 70-79 years. Females reported (33.75%) compared to (66.25%) males in the study.

Table 2: Distribution of studied sample according to the chemical composition of urinary tract stone.

Type of stone	Gender						
	Males		Females		Total		
	No.	%	No.	%	No.	%	P.V
Uric acid	10	18.87	4	14.81	14	17.50	0.016*
Calcium oxalate	40	75.47	13	48.15	53	66.25	
Uric acid +calcium oxalate	1	1.89	2	7.41	3	3.75	
Triple phosphate	0	.00	2	7.41	2	2.50	
Cystine	0	.00	1	3.70	1	1.25	
Calcium phosphate	2	3.77	5	18.52	7	8.75	
Total	53	100.00	27	100.00	80	100.00	

Significant association between type of stone and the gender of sample studied P= 0.016

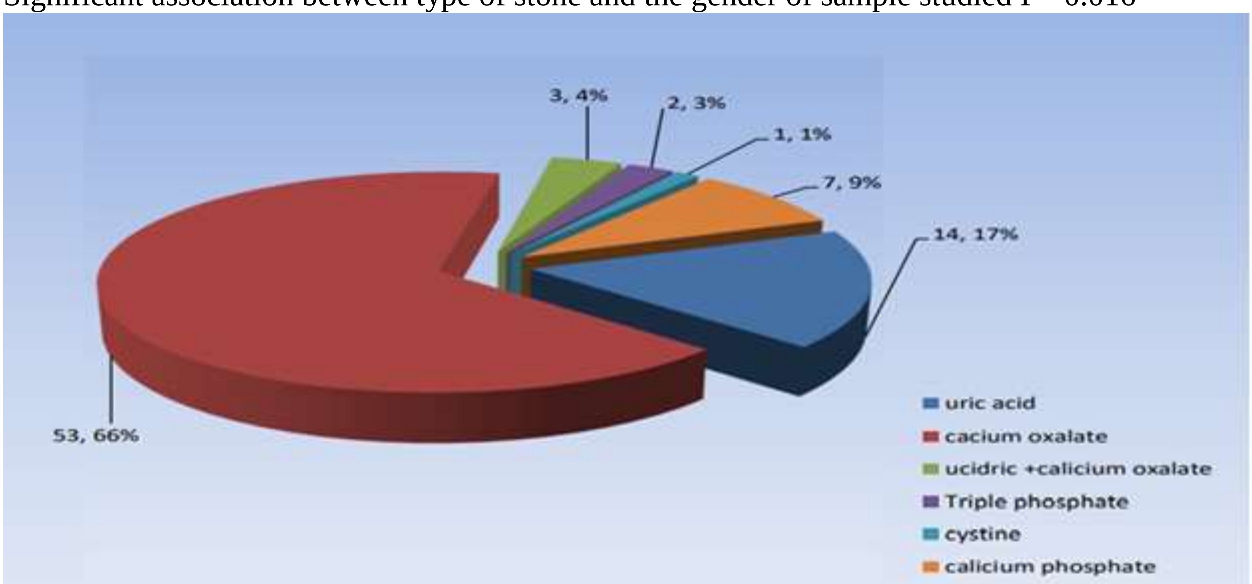

Fig. 1: Patients according to the percentage of chemical composition of the renal stone

The patients were admitted to the hospital with renal colic, hematuria, fever, chills and oliguria, 34 of the patients have one or more additional systemic diseases (4 with diabetes mellitus, 28 with hypertension, one patient with asthma and one patient with multiple chronic disease.

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According to the stone densities those determined by CT, the renal stones were divided into three groups, the first group; low density such uric acid stone their densities range 200-450 HU, the second group: medium density such cystine stone, struvite stone and mixed (calcium oxalate and uric acid) stone their densities range 450-600 HU and the third group: high density such calcium stone (oxalate or phosphate) their densities range 600-1700 HU.
According to PH of urine analysis, the renal stones were divided into two groups, PH of uric acid stones and cystine stone was less 6 and PH of calcium oxalate stones, struvite stones and calcium phosphate stones was more than 6.

Table 3: Relation of stone type with HU of CT and PH of urine.

	Type of stone	No.	Mean	Std. Deviation	F.test	P.V
HU of CT	Uric acid stone	14	258.5714	65.49893	39.542	0.0001*
	Calcium oxalate stone	53	824.2264	211.14920		
	Uric acid +calcium oxalate stone	3	500.0000	.00000		
	Triple phosphate stone	2	550.0000	17.67767		
	Cystine stone	1	487.5000	-		
	Calcium phosphate stone	7	1350.0000	115.47005		
	Total	80	747.2375	337.75484		
PH of Urine	Uric acid stone	14	4.9071	.31977	149.522	0.0001*
	calcium oxalate stone	53	6.5113	.25318		
	Uric acid +calcium oxalate stone	3	6.2333	.40415		
	Triple phosphate stone	2	7.3000	.70711		
	Cystine stone	1	5.5000	-		
	calcium phosphate stone	7	8.2000	.15275		
	Total	80	6.3525	.88946		

- Significance association between HU of CT and type of stone P=0.0001.
- Significance association between PH of urine and type of stone P=0.0001.

Table 4: Efficiency HU of CT for distinguishing uric acid stones from calcium stones for pure stone in comparison with PH of urine.

HU of CT For pure stone	PH of urine					
	Less than 6		More than 6		Total	
Uric acid stones 200 – 450	14	100.00	0	00	14	18.92
Calcium stones 600 – 1700	0	00	60	100.00	60	81.08
Total	14	100.00	60	100.00	74	100.00

Sensitivity HU of CT = 14/14 = 100%
Specificity HU of CT = 60/60 = 100%
PPV HU of CT = 14/14 = 100%

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NPV HU of CT = 60/60 = 100%
Accuracy HU of CT 74/74= 100%
In the table 4 show HU of CT predictive found the sensitivity is 100%, specificity is 100%, positive predictive value (PPV) 100%, negative predictive value (NPV) 100% and overall accuracy is 100% in pure stone.

A **B**

Fig 2: images of CT KUB for our samples studied. (A) Coronal CT scan show RT. renal stone size 23mm and 475 HU. (B) Axial CT scan show RT. Renal stone size 20 mm and 1050 HU.

A **B**

Fig 3: Images for type of stones for our samples studied. (A) Uric acid stones. (B) Calcium oxalate stones.

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DISCUSSION

Computed tomography is widely used to examine stones in the urinary system. In addition to the size and location of the stone and the overall health of the kidney, CT can also assess the density of the stone in Hounsfield units. HU a parameter generated from standard CT, are related to the density of the stone or structure of interest. In recent years, this has become an important diagnostic tool, for predicting the type of stone, urine pH, the presence of crystals, urease-positive bacteria in urine and a history of urinary stones have long been used to predict the composition of stones [15]. Stones are of different constituents including calcium oxalate, uric acid, magnesium, phosphate, ammonium and cystine [7]. The gender of patients was found 53 males and 27 females, while the percentage for male was 66.25% and female was 33.75%. A total of eighty patients with clinical and ultrasonographic diagnosis of urinary tract stone was included in the study. The age of patients ranges from 20 – 79 years old and the Mean ± SD age of study sample was 47.93±13.16. In this study, the females constitute 33.75% and the males 66.25%, show preponderance a male gender to have urinary tract stone, this results agree with Al-Athari et al. [19] who found that percentage of males with urinary tract stone (68.4%) compared to (31.6%) in females. Similar results also had been reported by Ma et al. [20] who found that percentage of males with urinary tract stone (65.8%) compared to (34.2 %) in females. Also this result is similar to what had been reported by Ouzaid et al. [12] who found that percentage of males with urinary tract stone (66%) compared to (34%) in females. According to our study, the middle age (40 – 60) years was more effected with urinary tract calculi, there is agreement between our study and study of Sorokin et al. [21], Soucie et al. [22] and Bultitude & Rees [23], these studies showed peaks of prevalence urolithiasis in the fourth to sixth decades of life. While in another study Ye et al. [24], it differs somewhat with our study found the maximum proportion of patients with urinary calculi were aged 31–60 years.

In this study, we found calcium oxalate stones were most common than other stones types 53(66.25%) followed with uric acid stones 14(17.50%), calcium phosphate stones 7(8.75%), mixed stones (calcium oxalate and uric acid) 3(3.75%), struvite stones (triple phosphate) 2(2.50%) and cystine stone in one patient (1.25) as shown in table 2 , this result agree with Journal & Al-khafaji [7] who found that calcium oxalate stone now account for more than 60% of all stones. Similar results also had been reported by Spivacow et al. [25] who found calcium-oxalate stone (66.7%), followed by uric acid stones in 16.5%, struvite stone (2.2%) and cystine stones (1%). Also this result is similar to what had been reported by Howles & Thakker [8] who found calcium oxalate stone (∼65%) but can also contain calcium phosphate stone (∼10%), uric acid stone (∼15%), cystine stone (∼1%).

In this study, show calcium stones have higher densities and uric acid stones have lower densities, there is agreement between our study and study of Atici et al. [26] and Mostafavi et al. [27], these studies reported that calcium phosphate stones consistently had the highest HU followed by calcium oxalate and magnesium ammonium phosphate stones (struvite), cystine and uric acid. Measurement of stone density, expressed in Hounsfield units, may be used to assess stone composition, with higher values suggesting calcium stones and lower values uric acid stones [9]. The HU measurements of the various urinary stones at 120 kV usually fall under the following range: Uric acid stones are 200–450 HU, calcium phosphate stones are 1200–1600 HU [28]. Uric acid stones are typically 200–450 HU, whereas calcium oxalate stones are 600–1200 HU [14], intermediate values may be due to mixed calcium/uric acid stones [9]. Struvite 510 to 600 HU [29] and this considered agree with our study, there was an overlap between the HU values of cystine and uric acid stones [15], the diagnosis of cystine stones is also guided by

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laboratory and epidemiological data (Brand's test, urinary pH, crystals, uricosuria, patient age) [30].

There is significance association between HU of CT and type of stone and there is significance association between PH of urine and type of stone as shown in table 3.

The comparison of finding for HU of CT with PH of urine, the sensitivity of HU results in predictive of uric acid stones was (100%) that mean HU of CT was able to assessed all patients with uric acid stones correctly. The specificity of HU results in predictive of calcium stones was (100%) that mean HU of CT was able to assessed all patients with calcium stones correctly. Positive predictive value (PPV) was (100%) that mean all those predictive as uric acid stones by HU of CT was (100%) being uric acid stones by PH of urine and negative predictive value (NPV) was (100%) that mean all those predictive as calcium stones by HU of CT being calcium stones by PH of urine and overall accuracy was (100%). Two patients had struvite stones and one patient had cysteine stones, these stone types were not included due to small numbers. An additional three patients were excluded due to mixed stone types as shown in table 4. This results agree with Lombardo et al. [31] who found the sensitivity and specificity were 100% in differentiating uric acid from calcium stones. The accuracy for distinguish uric acid stones from calcium stones were 100% in this study, this result agrees with Primak et al. [32] who showed that accuracy 92-100% differentiating uric acid from non-uric acid stones. Similar results also had been reported by Spettel et al. [33] who found the combination of HU and pH criteria for uric acid stone and calcium stone resulted in a sensitivity : 86%, specificity : 98%, PPV : 80% and NPV : 98%. Also, this results is agree with Rompsaithong et al. [13] who found there were sensitivity of 88.9%, specificity of 96.7%, positive predictive value of 88.9% , negative predictive value of 96.75% and accuracy of 94.8% in differentiating uric acid from calcium stones, that is slightly lower than with the recorded by our study.

Urinary pH is one of the major determinants of kidney stone formation, In general, a pH below 5.5 increases the risk of uric acid stone formation, and a pH above 6.0 increases the risk of calcium stones [34].

CONCLUSION

All urinary calculi examined were clearly visible on CT regardless of chemical type. We found the chemical composition of urinary calculi can be accurately predicted by CT using the HU parameters. HU measurements at CT scan may help to predict the stone composition, they provide differentiation of high dense (calcium), medium (struvite and cystine) from low dense (uric acid) stones. We found HU parameter in computerized tomography can distinguish uric acid stones from calcium oxalate stones with high accuracy were 100% in comparison with PH of urine examination.

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