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USE OF NONENHANCED COMPUTED TOMOGRAPHY IN PREDICTING RENAL STONE COMPOSITION

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ABSTRACT

Background: Urolithiasis is truly one of the most painful medical condition afflict human being, there are many types of renal stones, one of the most important factors on which urolithiasis treatment depend on is the chemical composition of the stone, prediction of renal stone composition before treatment will help the urologist to choose the suitable line for treatment. Non-enhanced CT offer important information about existence, size, location and predict the chemical composition of the renal stone. Aim: correlation between renal stone composition and Hounsfield Unit and Hounsfield density in non-enhanced CT. Patients and methods: This prospective study was conducted during the period from August 2014 to September 2015 on 50 patients, referred from the Urology department, each has single renal stone of more than 10mm in diameter detected by ultrasound, unenhanced CT scan and KUB were done for all patients, after treatment the stone specimens collected and send for chemical analysis, the chemical composition of each stone was compared with its HU and HD and statistically evaluated. Results: The 50 renal stones were classified in to six groups according to the laboratory results: 14 pure Calcium Oxalate (CO), 10 pure uric acid (UA), 12 struvite (STR), 7 Calcium Oxalate + Hydroxyapatite (CO+HXA), 3 Calcium Oxalate + Hydroxyapatite + Struvite (CO+HXA+STR), and 4 Calcium Oxalate + Uric acid(CO+UA) stones, calcium containing stones were about 56% in the studied samples, a significant relationship (P. value < 0.001) was found between the types of the renal stone and their HU, mixed CO + HXA stones were the highest value (1280 – 1464),then pure CO (1080 - 1260), then mixed CO + HXA+ STR (830-980), then the Pure STR stones which show an overlap between their HU (533 – 734) and mixed CO + UA stones HU (396 – 586), finally the pure UA stones which are the least HU stones in our study

(215 – 342),HD value was obtained from dividing the HU by stone diameter, the result was ranging from 18 – 69.4, various types of stones show significant relationship with their HD (P value < 0.001), the pure CO stones show the highest HD (59.5) while the pure uric acid stones show the lowest HD (20.5), still there was overlap between STR and mixed CO + UA stones where they show HD of 23.2-32 AND 23. 3-25. 6 respectively. Conclusion: Non-enhanced CT can determine the chemical composition of most renal stone types by measuring the HU and HD of the stone.

INTRODUCTION

Urolithiasis is truly one of the most painful medical condition afflict human being, its prevalence is increasing across the world in the last 30 years. (1) FIG. 1 shows the high incidence regions across the world in what is called a stone belt. In the United States, the prevalence has been estimated at 10% to 15%, (2) while 10% in United Kingdom. The prevalence of renal stones varies, it also correlates with affluence. (3)

previously most studies report that males are affected 3 times as frequently as females. Testosterone may cause increased oxalate production in the liver (predisposing to CO stones) and women have higher urinary citrate concentrations (citrate inhibits CO stones formation). (4)Nowadays the gender gap is closing where the new studies in USA reports that the ratio is 1.3-1 (5).

Urine pH in normal individuals shows variation, pH 5–7. After a meal, pH is initially acid because of acid production from metabolism of purines (nucleic acids in, for example, meat). This is followed by an alkaline tide, with pH rising to > 6.5. Urine pH can help establish what type of stone the patient may have and can help the urologist and patient in determining whether preventative measures are likely to be effective or not. *Calculi that contain calcium are radiodense. Sulfur-containing st*ones (cystine) are relatively radiolucent on plain radiography. Radiodensity of stones in decreasing order are calcium phosphate > CO > STR (magnesium ammonium phosphate) >> cystine. Completely radiolucent stones (e.g., UA, triamterene, indinavir) are usually suspected on the basis of the patient's history and / or urine pH (pH < 6: gout; drug history: triamterene, indinavir), and the diagnosis may be confirmed by ultrasound, computed tomographic urography (CTU), or magnetic resonance urography (MRU). (6)

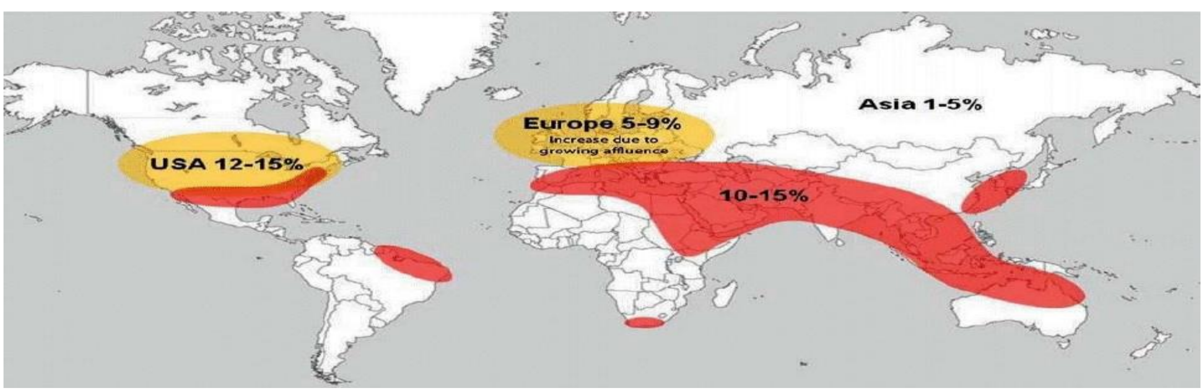

FIG. 1 The so-called stone belt (red) extends all the way around the world and is characterized by urinary stone prevalence of 10 to 15 %. (2)

Aim of study:
Studying the relationship between renal stone composition and Non-enhanced CT Hounsfield unit and Hounsfield density

PATIENTS AND METHODS

Patients:

This prospective study was conducted during the period from August 2014 to September 2015 at the radiology department in Al-Imamain Al-Kadhmain medical city and includes 50 patients. The 50 patients were referred from the Urology department all with single renal stone of > 10mm in diameter detected by ultrasound, unenhanced CT scan and KUB were done for all patients, then the stone specimens collected and send for chemical analysis,

Exclusion

1. Patients with renal stone of less than 10mm maximum diameter.
2. Patients with multiple renal stones (unilateral or bilateral).
3. Patients who didn't collect their renal stones after treatment.

Statistical analysis:

Data are presented as means, SD, and percentage. Categorical data are expressed as frequencies and were compared with Pearson's Chi-square and F test. Continuous variables are presented as the mean SD and were compared using ANOVA (analysis of variance). A probability (P) value of less than 0.05 was considered statistically significant. Data were analyzed by appropriate computer software (SPSS. Version 20

RESULTS

There were 50 patients enrolled in this study. Their demographic results are shown in the following:

Age and gender distribution:

The mean age of the studied group was 42.4 – 14.7 (range: 14 – 71 years), males were 36/50 (72%) and 14/50 (28%) where females, male to female ratio of (2.5:1), as shown in FIG. 1.

Male = 36
Female = 14
M:F = 2.5:1

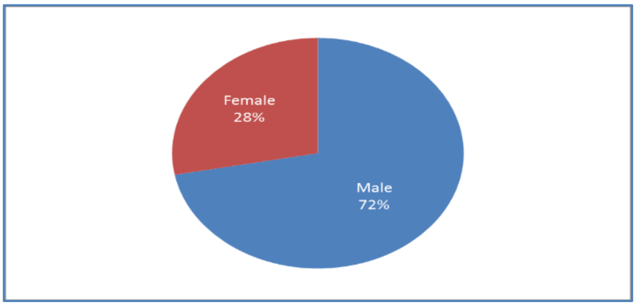

FIG. 2. Age and gender distribution

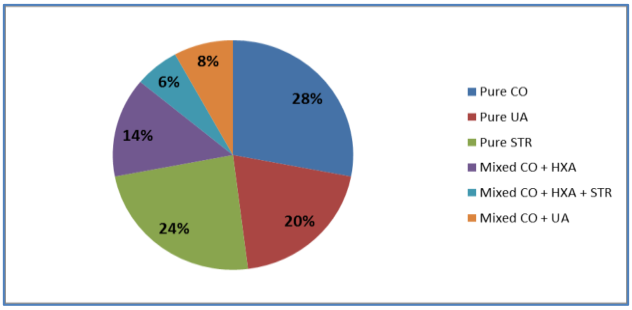

FIG 3 Percentages of stone types

CT attenuation and density.

Calculi were classified in to six groups according to the laboratory results:14 pure CO, 10 pure UA , 12 STR, 7 CO + HXA, 3 CO + HXA + STR, and 4 CO+ UA stones, the distribution and percentage of each type are shown in table 1 and FIG 2, calcium containing stones were about 56% in the studied samples.

Table 1 Stone types of distribution and percentage

Stone type	**No.**	**Percentage**
Pure CO	14	28.00%
Pure UA	10	2.20%
Pure STR	12	2.20%
Mixed CO + HXA	7	12.20%
Mixed CO + HXA + STR	3	4.20%
Mixed CO + UA	4	6.20%
Total	50	100.00%

Regarding the absolute Hounsfield units (HU) was ranging from 215 to1464, there was a significant relationship (P. value < 0.001) between the types of the renal stones and their HU, different types of stones show different ranges of HU as shown in table 5 and FIG 7, from the most dense to the least dense stone, mixed CO + HXA was the densest stone (1280 – 1464), then pure CO (1080 -1260), then mixed CO + HXA + STR (830-980), then the Pure STR stones show an overlap between their densities (533 – 734) and mixed CO + UA stones (396 –586), finally the pure UA stones which is the least dense stones in our study (215 –342). Mixed CO + HXA, pure CO and Mixed CO + HXA + STR are the highest HU values and can be differentiated from all other stone types, pure UA stones is the lowest HU and can be differentiated easily from other types, while mixed CO + UA stones and STR stones shows no wide difference between their HU values, but generally the later show higher values where there were 8 of 12 STR stones of more than 600 HU while no any mixed CO + UA stones exceeding 600 HU.

Table 2 Comparison of HU, HD, and stones diameter of various stone types

Stone type		HU		Dia	Stone meter(mm)			HD	
	min	max	Mean	min	Max	Mean	min	Max	Mean
Pure CO	101	1260	1183.5	18	23	20	50.7	96.4	59.5
Pure UA	205	342	297.7	10	18	14.6	18	22.4	20.5
Pure STR	533	734	636.8	18	28	23.6	23.2	32	27.1
Mixed CO + HXA	1280	1464	1368.6	26	32	29.7	43.3	49.2	46.1
Mixed CO + HXA + STR	830	980	893.3	23	28	25.3	33.2	35	35.3
Mixed CO + UA	396	586	508.5	17	24	20.7	23.3	25.6	24.4
P value		< 0.001			0.081			< 0.001	

Stone size

Stone sizes were ranging from 10mm to 32mm (The average size 21.54mm), there was no significant relationship between stones type and their diameter (P value = 0.081), where a wide overlap between various types seen, but overall the pure UA stones are the smallest sizes (mean 14.6mm), while the mixed CO + HXA stone where the largest stones of about 29.7mm mean diameter, as shown in table 2.

The Hounsfield Density (HD):

The HD was ranging from 18 – 69.4, stones types show significant correlation with their HD (P value < 0.001) as shown in table 5 and FIG. 9, the pure CO stones show the highest HD (mean 59.5) while the pure uric acid stones show the lowest HD (18), still there was an overlap between STR and mixed CO + UA where they show HD of 23.2-32 and 23.3-25.6 respectively.

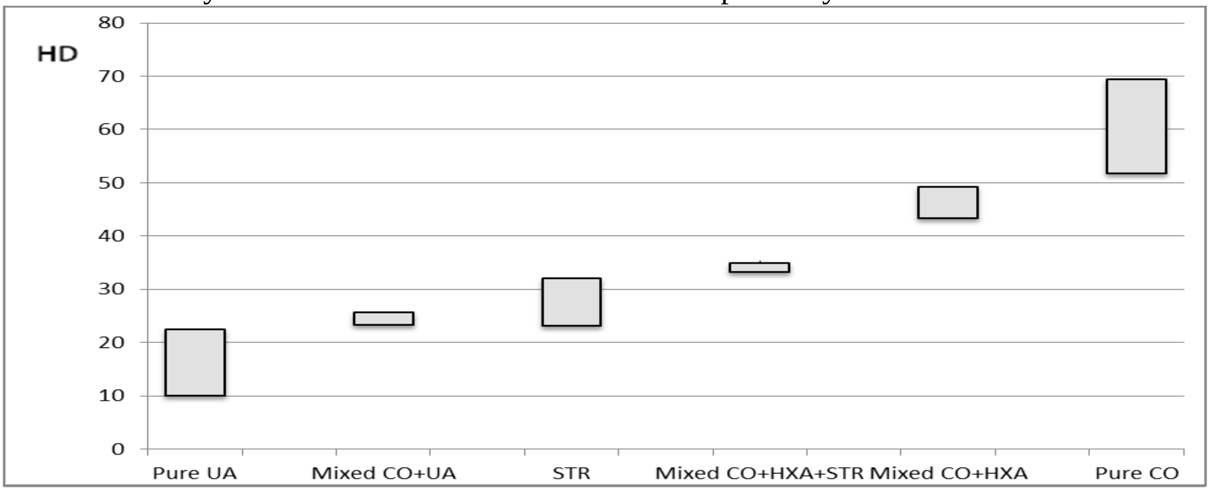

FIG. 4 Comparison the HD values in different renal stones

Through studying the three parameters (HU, HD and stone diameter) in both genders we found a positive relationship between the gender and both HU and HD, but there was no significant relation between patient gender and stone diameter where a similar stone diameter reported in either gender (P value 0.658), generally a higher HU and HD values were reported in females (P value 0.024), these relationships displayed in table3.

Table 3 Comparisons the differences of stone diameter, HU, and HD in both genders

The parameter	Female	Male	P value
Stone diameter (mm)	21.1 3.1	21.7 5.9	0.658
HU	976.5 341.9	772.5 403.9	0.024
HD	46.6 16.9	34.4 14.5	0.01

Stones appearance in KUB:

Regarding the appearance of the stones in KUB, there were 12 radiolucent (24%) and 38 radiopaque stones (76%), as shown in table 7. There were a significant relationship (P value < 0.001) between our three parameters and stone appearance in KUB, radiopaque stones were larger in size and show higher HU and HD than radiolucent stones. The higher radiolucent stone HU was 396 which was a mixed CO + UA. Stone while the lowest radiopaque stone HU was 533 which is STR stone.

Table 4Comparison the stones HU, HD and diameters of both radiolucent and opaque stones

The parameters	Radiolucent stones	Radiopaque stones	P value
Stone diameter (mm)	15.3	23.5 4.1	< 0.001
HU	323.8 67.5	989.4 309.3	< 0.001
HD	21.2 1.9	43.1 14.9	< 0.00

The parameter Stones location within the kidney:

There were 20 pelvic stones, 12 mid, 9 lower and 9 upper calyx stones, no significant relationship was found between stone location and its HU (value0.079) also with its HD (P value 0.649), while there was a significant relationship between the position of the renal stone within the kidney and its diameter, the pelvic stones where the largest & densest stones,

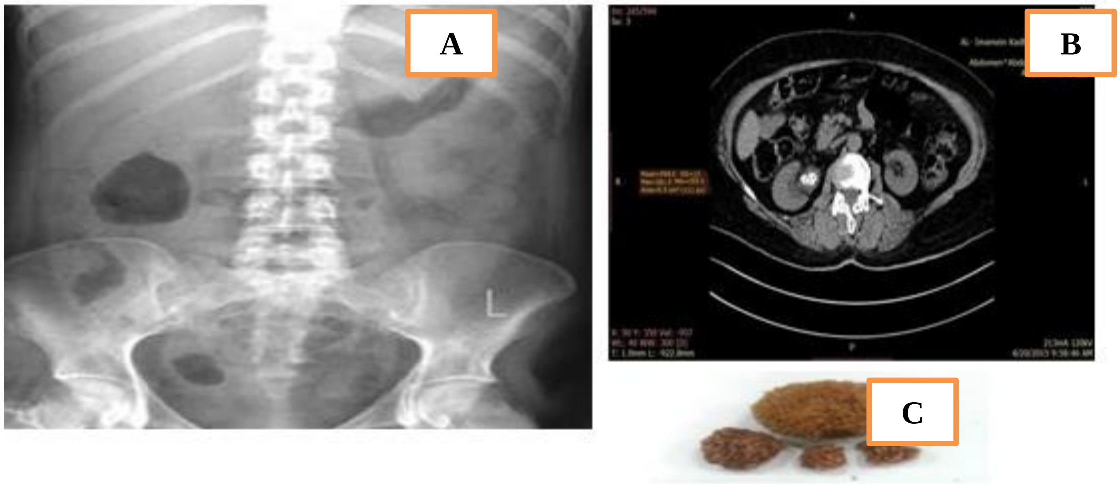

FIG 5. 71 years old female with right renal pelvic stone

A. KUB show unremarkable finding (no radiopaque stone).

B. Axial CT scan at level of kidneys show hyperdense renal stone in Rt renal pelvis, the HU was 268.5 C. The stone was pure uric acid

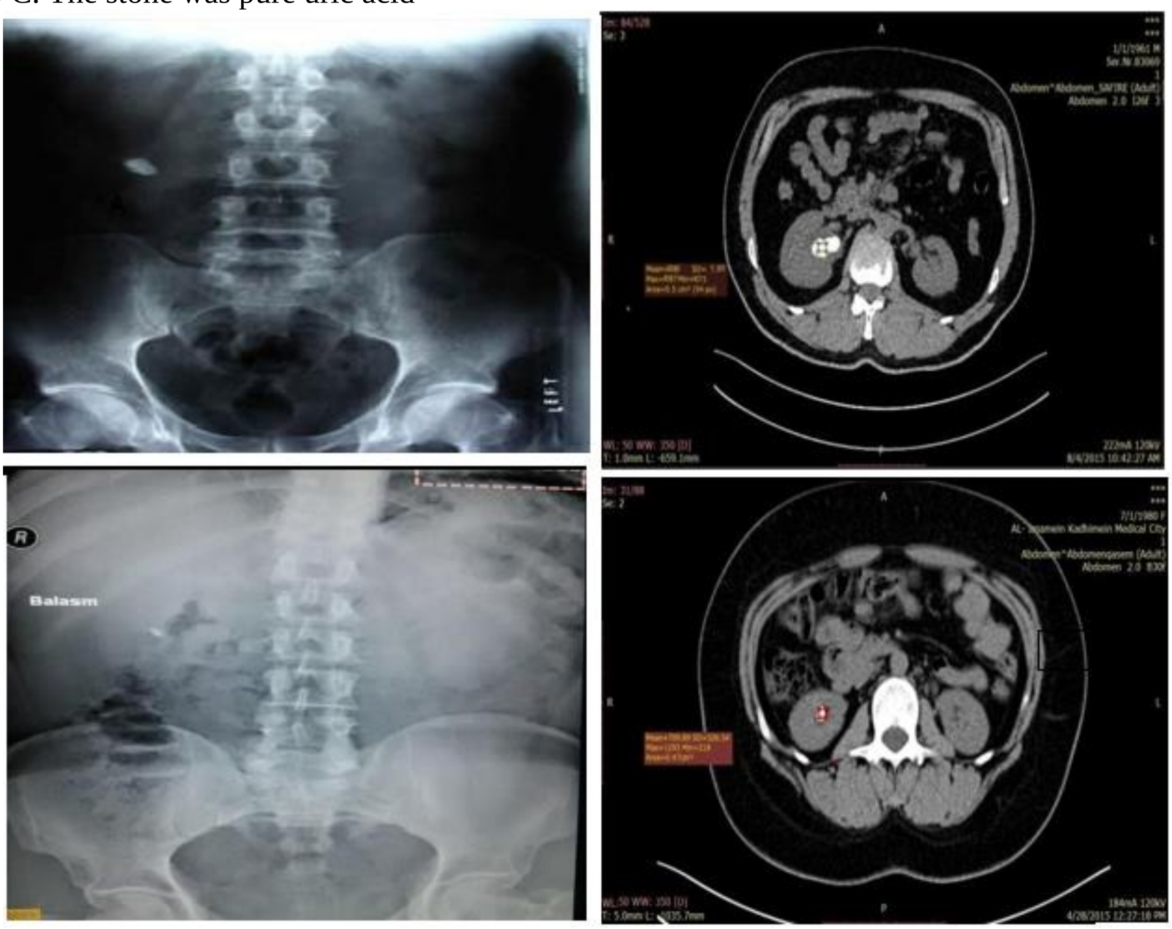

FIG 6. Imaging findings of four patients with renal stones

DISCUSSION

Unenhanced helical CT accurately diagnoses urolithiasis. CT is the reference standard for the diagnosis of nephrolithiasis and in the evaluation of patients with acute flank pain. (7),(8),(9). It is available, rapid, and accurate, with one series reporting 96% sensitivity,99% specificity, and 98% accuracy in the diagnosis of urolithiasis. Very important information in treatment of renal stone can be acquired from

CT scan as stone size, location, associated congenital abnormality and its composition. (10)
By using thin collimation scan we can reduce the partial volume inaccuracies,(11) but this will expose the patients to higher radiation dose, this was reported by Saw, *et al* (12) who reported that using a smaller collimation (2mm) size when scanning urinary stones permits better accuracy in the prediction of composition, so we chose the 5mm collimation which is used ordinarily and reconstructed the images to 2mm thickness. Several studies were conducted in the last 20 years to determine the chemical composition of stones using CT. Some authors reported promising results with the ability to identify all stone types (13,114,15,16 and 17). In this study a significant positive correlation found between the HU and renal stone types,display five previous studies shows results similar to our results, the patients and methods in all the five studies were mentioned, in spite of differences in CT scanners, collimations and the stones surrounding media, the HU of the common stones types appear to be in the same range. Tthe HU of calcium containing stones generally is more than 1000 HU. In our study calcium containing stones show HU of more than 800 and HD of more than 33, but (18) reported HU of around 900 UA stones were ranging 215 - 342 HU in our results while it shows little higher HU in the other studies (> 400 HU). This may result from the separation between calcium containing uric acid stones and pure uric acid where we put these stones in different group types while the previous studies consider these as one type.Our study agreed with Marchioro G, *et al* (19) who studied 76 stones with CT scanning at 120 Kv and analyzed their stones by chemical analysis and identified a specificity of 91% and 96%, respectively for UA and phosphates stones,
The classified stones in to three major types:

UA pure and mixed with CO (352 – 594 HU)
Pure CO (460 – 942 HU)
Mixed CO with STR and phosphate (502 – 1205 (HU),

Nakada, *et al.* (20) analyzed 129 stones in an in vivo setting. In 99 patients, they identified 82 calculi predominantly composed of CO and 17 calculi predominantly composed of UA and concluded that using peak attenuation measurements and the attenuation/size ratio (HD) of urinary calculi from NCCT enable them to differentiate between UA and CO stones. Deveci, *et al.* (21) found that using an absolute CT value at 120 kV, all types of renal calculi could be differentiated from each other. The pure stones from the least to the densest were as follows: UA, STR, cystine, calcium phosphate, and CO this was the same finding in our study.Some other studies reported limitations in identification of stone composition using CT. Saw, *et al* (22) studied 127 stones at 1, 3 and 10 mm collimation and could differentiate the stone types studied except for brushite from hydroxyapatite. Grosjean, *et al* (23) showed that an overlap between different types of stones prohibited a reliable determination of chemical composition by two subsequent scans and this was explained by the movement of the kidneys as a result of respiration (i.e. partial volume effect). Hidas, *et al* (22) could not distinguished STR stones and the subtypes of calcium stones; this may be due to real chemical overlap between stone compositions and differences in absorption among patients of different sizes.

The HD showed a significant relationship between various types of renal stones ($P < 0.001$). The highest values were the pure CO stones while the pure UA stones where the lowest, still there where an overlapping between the HD of mixed CO + UA and STR stones. Motley G, *et al* (23) studied the HD of 100 renal stones with 7mm collimation and reported that significant differences were noted between the mean HD of calcium (105 43) and uric acid (50 ± 24) stones (P = 0.006). Shahnani, PS *et al* (24) stated a strong relationship between the HD and the stone composition in 180 urinary stones from patients seen at Shariati, Kashani and Alzahra CT centers in Iran (CT collimation 6mm) and reported that a relationship between composition of stones and HU ($P = 0.001$), HD ($P <0.0001$) were seen , the HD of CO were 49-68 (our result 51-69) , STR stones HD were 20-38 which was similar to our result 23-32, while UA stones show higher HD (23-41) than our result (18-25), Shahnani, PS *et al* (25) found no overlap between calcium oxalate and others, except calcium phosphate and their results disagreed with our study about relationship between stones composition and size, were they found positive relation (*P value=0.001*), these differences may be due to the wider collimation in both studies and involvement of small size stones due to the increase in HU inaccuracies that result from partial volume effect, Predicting the stone composition is very important for the urosurgeon sincemany types of stones resist ESWL while ESWL monotherapy is more likely to be effective against other stones, Nakasato T, ET al report that renal stone less than 815 HU easily treated with monotherapy ESWL than those with a higher HU, Ouzaid I, *et al* (25) evaluated 50 patients with urinary calculi of 5-22 mm undergoing ESWL, all patients had NCCT at 120 kV and 100 mA , they report that stone-free rate for stones of < 970 HU was 96% vs. 38% for stones of ≥ 970 HU (P< 0.001), in line with that (in our study) these stones which show HU > 900 were the Pure CO and Mixed CO + HXA assumed to be resist to ESWL and another treatment option should be tried, which was the mattered in these 21 stones, ESWL and medical treatment were failed , and all of which treated successfully by PCNL.As shown in table 6, renal stones in female patients were of higher HU and HD than stones in male patients, the P values were statistically significant (0.024 and 0.012 respectively) this may due to lack of daily fluid intake more in female patients which agreed by Charles D, *et al* (26). Michael EC, *et al* (27) proposed cut-off value of 610 HU to differentiate between lucent and opaque stones. This agreed with our result where the higher radiolucent stone HU was 396 which was a mixed CO + UA stone while the lowest radiopaque stone HU was 533 which is STR stone.Regarding the limitation, we found that not all stone types were identified in our study. The chemical analysis of the stone cannot differentiate the subtypes of calcium stones.

Table 5 comparison between this study and previous studies results:

Parameter	1983(44)	1983(45)	1997(46)	2003(42)	2006(47)	2014(43)	2006(47)
CT scanner	Somatom	GE8800	HiSpeed	Somatom	Somatom	Somatom	Somatom
Collimation	2	5	1	3	0.75	3	5
Surrounding medium	Water	Water	Air	Pig kidney	Jelly	Human kidney	Human kidney
Stones Number	80	63	102	100	241	253	50
Calcium oxalate	1023	1273-193	1620	837	1216	624-309	1080-1260
Struvite	651	948	666	563	461-117	687±333	533-734
UA	540	448	409	386	437	385±176	215-342

CONCLUSION:

Non-enhanced CT can determine the chemical composition of most renal stone types by measuring HU and HD, there is no relation between the size of the stone and its type.

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