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Correlation and predictive value of ultrasound twinkling effect of Urolithiasis with chemical composition of calculi

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Abstract

Background : Although helical CT enjoys the highest sensitivity and specificity levels in detecting Urolithiasis, latest Sonography techniques combined with radiography can be a cost effective method of evaluating renal calculi with equivalent sensitivity and specificity. In evaluating Urolithiasis, if the composition of the stone being studied could be predicted, that knowledge could vastly influence the choice of treatment modality, follow-up schedule and preventive measures against recurrence.

.**Methodology**: This prospective analytical study evaluated Urolithiasis of 30 patients by radiography and sonography to correlate specific findings in the diagnostic methods with the chemical composition of the stones.

Result: We were able to evaluate all the Urolithiasis cases by using plain X-ray and ultrasound with a sensitivity and specificity of 100% in the study group. In sonography, we could visualise the 'Twinkling Artifact' effect in almost all the patients. On grading the twinkling artifact and comparing our various measurements with the chemical composition of the stones, we detected that the twinkling artifact has a significant correlationship with predominance of COM in the calculi.

Conclusion: Sonography and Radiography are reliable diagnostic modalities for evaluation of Urolithiasis and the twinkling artifact effect in sonography can be used to predict the nature and composition of the stone which can assist in choosing further mode of treatment.

Key words: Ultrasound**,** Twinkling Effect, Urolithiasis, Calculi

Introduction

Urinary calculi (Urolithiasis) are the third most common affliction of the urinary tract, exceeded only by urinary tract infections and pathologic conditions of the prostate. Many treatment modalities including surgical intervention, endoscopic methods, medical agents, and extracorporeal shock wave lithotripsy (ESWL) have been used for urinary calculi. With the widespread use of ESWL, urologists noticed that the fragmentation rate of urinary tract stones correlates with stone location, size and most importantly, fragility.

Radiologic studies for urolithiasis include plain radiography, intravenous urography (IVU), sonography and computed tomography (CT). Intravenous urography following plain radiography has been a traditional radiologic workup sequence. In the past several years, thin-section non–contrast-enhanced CT has been the reference standard for diagnosing urinary tract calculi in adults .Non–contrast-enhanced CT has higher sensitivity and specificity than either sonography or IVU for detecting ureteral stones.

In recent years, new sonographic equipment and technologies have been developed that improve image resolution and lessen artifacts. The sensitivity and specificity of sonography has been reported to be as high as 93% and 95% respectively, by definite demonstration of lithiasis with new sonographic equipment and technologies. When combined with plain KUB radiography, Sonography can replace helical CT as the cost effective diagnostic modality of choice for detecting and diagnosis of urolithasis. Additional useful modalities for diagnosing urolithiasis by sonography have been reported, such as TWINKLING ARTIFACTS and the application of endocavitary and high-frequency transducers for small calculi, .

In the treatment of patients with urinary tract calculi, symptomatology of patients, stone size, and stone composition are factors that influence therapy. Accurate preoperative prediction of composition of urinary stone remains a challenge for the urologist.

Knowledge of the stone composition is important since it influences the choice of treatment modality, follow-up schedule and preventive measures against recurrence.

Stone characterization is becoming more even important with the development of percutaneous nephrostolithotomy. Until now, the main criteria for choosing between this procedure and the extra corporeal shock wave lithotripsy were the size and location of calculi. However, small dense calculi are difficult to fragment with extracorporeal shock wave lithotripsy and probably are more effectively treated by nephrostolithotomy. Urate, calcium oxalate monohydrate (whewellite) and cystine stones are hard and less responsive to treatment with extracorporeal shock wave lithotripsy (ESWL), whereas pure or predominantly calcium oxalate dihydrate stones are much more fragile and hence are good candidates for extracorporeal shock wave lithotripsy.

Currently stone analyses using methods such as infrared spectroscopy, x-ray crystallography and polarizing microscopy are done for stone fragments retrieved from the patient after treatment. However, what is advantageous is preoperative knowledge of stone composition while the stone is still in situ.

The efficacy of lithotripsy is based on several parameters, such as the size and the location of calculi within the pyelocaliceal system, Several studies have emphasized the role of the chemical composition of stones in the predisposition to fragmentation, the so-called "stone fragility." The fragility of the stones of different crystallographic composition was known to make a decreasing order of fragmentation for struvite (magnesium ammonium phosphate hexahydrate), uric acid, calcium oxalate dihydrate (COD), calcium oxalate monohydrate (COM), and finally cysteine. Thus stones composed entirely of calcium oxalate dihydrate are much less resistant and require fewer shock waves than 100% calcium oxalate monohydrate stones.

Several techniques have been introduced for detection of stone composition including tomodensitometry , dual-energy radiographic bone densitometry , non-contrast spiral computerized tomography , Tc-99m bone scan , low-angle X-ray scattering (LAXS) , pulsed dye laser and infrared analysis . We should note that these modalities are not widely available for use in a typical Indian hospital setting.

The macroscopic aspect and color of stones, which are visible during pyeloscopy, are known criteria for guiding percutaneous endolithotripsy. However, to preoperatively predict the efficacy of endolithotripsy, other authors have tried to establish correlations between the radiological pattern of stones and their composition.

Sonography is one of the primary techniques for diagnosing calculi, localizing them, and guiding extracorporeal lithotripsy. Associated with the standard B-mode sequence, color-flow sonography may provide added functional information about the degree of obstruction, based on analysis of ureteral jets and—with more controversial results—on the determination of intrarenal resistivity indexes , . Recently, a color artifact called the "TWINKLING ARTIFACT" has been described behind calcified matter in various tissues and, in particular, behind urinary stones . This artifact, which results from complex physical mechanisms, is related to the irregularity of the surface of calcifications, and the technical parameters used during scanning were not thought to affect it. The twinkling artifact appears as a random color encoding behind the stones in the region where shadowing would be expected on gray-scale images.

Stone characterization is becoming more important with the development of percutaneous nephrostolithotomy. Until now, the main criteria for choosing between this procedure and the classical extracorporeal shock wave lithotripsy were the size and location of calculi. However, small dense calculi are difficult to fragment with extracorporeal shock wave lithotripsy and probably are more effectively treated by nephrostolithotomy. Pure monohydrate calculi are extremely dense and resistant, whereas pure or predominantly calcium oxalate dihydrate stones are much more fragile and consequently are goodcandidates for extracorporeal shock wave lithotripsy. This parameter is still underused by urologists [Dretler SP et al.64] even though, during endoscopic examinations, the two types of calcium oxalate stones can be distinguished on the basis of their morphologic patterns and color—black for calcium oxalate monohydrate and yellow for calcium oxalate dihydrate. Dretler and Polykoff showed that the radiographic patterns of stones can be correlated with four types of calcium oxalate stones. However, these patterns were found to be reliable only for stones greater than 1 cm in diameter, and such analysis is impossible when the stone is superimposed on bony structures. The twinkling artifact with color-flow sonography is not limited by the size of the calcification and can be found even though sometimes it is slight and spread out within tissues.

Aims & Objective

In this study, we attempted to use ultrasonography combined with plain KUB radiography to characterise and predict the composition of the stones. In this study we compare and correlate the predictions done on 30 patients with the actual stone analysis results to find if sonography with radiography can indeed be relied upon to provide in vivo information about the stone compositions.

The Aim of this study was to evaluate and determine the correlation between Sonographic and Radiographic evaluation of Nephrolithiasis and the chemical composition and morphology of the calculi.

Subjects and Methods

The study was approved by both the Scientific Research Committee as well as The Human Ethics Committee of Mahatma Gandhi Medical College and Research Institute. All participating volunteer patients provided full informed consent for participation in the study.

100 Patients were chosen at random using a randomization table generated with IP/OP numbers from around 600 consecutive patients referred with clinically suspected urinary tract calculi from various departments, especially Urology and Surgery. These patients underwent screening

sonography. Of the 100 patients, 62 were subsequently confirmed with urolithiasis and out of 62, 48 patients were willing to undergo Operative surgery at the Department of Urology. Out of the 48 patients, 30 patients provided informed consent and were enrolled into the study. Detailed ultrasonography and KUB radiography was done and recorded. The urinary calculi of these patients were retrieved post-operatively and sent for X-ray diffraction crystallography and analysis.

Using a standardized sonographic scanning technique, all the patients were screened and studied for presence of a calculus defined as a constantly echogenic lesion clearly located within the Kidney, ureter, urinary bladder, or urethra. Color Doppler imaging was used in all the Calculi shown by sonography to determine the presence or absence of a twinkling artifact.

Twinkling Artifact

In 1996, "TWINKLING ARTIFACT" was described by Rahmouni et al. as an artifact composed of rapidly alternating multicolour pixels in perpetual motion. In their words, they described the phenomenon as 'New color Doppler ultrasound (US) artifact that manifested as a rapidly changing mixture of red and blue behind a strongly reflecting structure'.

The twinkling artifact is generated by a strongly reflecting medium, and occurs behind the near-field interface of the object for a finite distance, often beyond the actual object resulting in the generation of this artifact. The twinkling artifact, observed in our study on ultrasound with a curvilinear transducer of 3.5 to 5 Mhz frequency to occur as a distinct shadowing along the lower contour of renal stones extending for a few cms depending upon the composition, site and density of the stones. The artifacts can be seen as a series of polychromatic pixels with a twinkling effect that lends it its name, quite like a comet tail.

For visualization of twinkling artifacts, focal zones were always placed near the depth of the calculi with careful control of the B-mode gain settings. For color Doppler sonography, a red-and-blue color map was used, and the color window size was adjusted to cover the concerned lesion and adjacent tissue. The presence of a color signal was assessed relative to adjacent soft tissue. When we found a calculus, we recorded the location, largest diameter, post acoustic shadowing and presence of a twinkling artifact.

Grading of 'Twinkling artifact'

The twinkling artifact was graded 0 when absent, 1 when present but occupying a portion of acoustic shadowing, and 2 to 3 when it covers upto half of the acoustic shadow and 4 when it extends beyond half of the shadow, forming a 'comet tail'.

Radiography

Unenhanced urinary tract radiographs were obtained with conventional film from a GE-500 MA machine. A single anteroposterior acquisition of the whole urinary tract was obtained with the patient in supine position. Bowel preparation was done with laxative, given one day in advance in order to dispel bowel gas and contents. The Patients were advised overnight fasting for 6-8 hrs. till radiography.

In the resultant radiograph images, the stones were pinpointed, their size and location recorded along with the following parametric information: characteristics of the stone - homogeneity, opacity, and comparative density with reference to the adjacent 12th rib or spinal transverse process.

X-**Ray Diffraction Crystallography**

The urinary stones of all the study subjects were collected post operatively and placed in a plastic container which was labeled carefully. The stones were washed with sterile water to remove any blood or attached tissue and dried on a filter paper. The external appearance was noted as smooth or rough and weighed.

They were packed and sent to the Crystallography Laboratory of the Department of Physics, University of Pondicherry, for further analysis by X-Ray Diffraction to assess the chemical composition of the stones.

Data Handling

All the data from the patients, diagnostic notes, sonography and radiography reports, XRD reports from Laboratory, etc were collected and entered into a MS Access Database. The data was checked for indiscrepancies and exported to SPSS program (version 17) for statistical analysis.

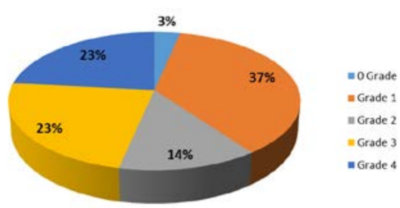
Results

Nature of the stones

From the analysis of the stones obtained post-surgery, it was found that 7 of the stones were smooth and the rest 23 were identified as rough.

Twinkling artifact

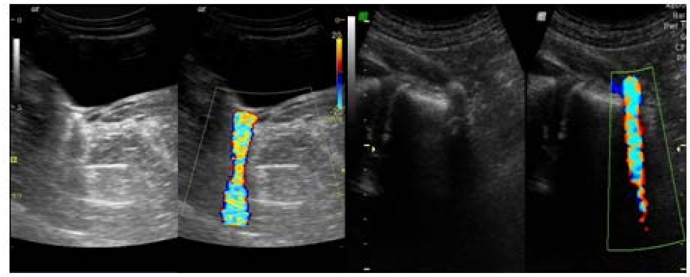
Post acoustic shadowing was positive in all the cases. The Twinkling artifact was visualised and recorded in 29 cases out of 30 with the following statistics on grades:



11 cases (37%) showed a Twinkling Artifact of Grade 1, while 4 (14%) exhibited grade 2 artifacts. Grade 3 and grade 4 artifacts were seen in 7 (23%) cases each.

Chemical composition of stones

All the stones retrieved after the operation and send for X-Ray diffraction analysis showed that the stones were predominantly either calcium oxalate dihydrate (COD), calcium oxalate monohydrate (COM) or a combination of both to varying degrees.



Statistical Analysis of all the Characterisation data obtained from Sonographic and radiographic evaluation of nephrolithiasis were tested for correlation with the chemical character of the calculi. Pearson 2 tailed Correlation was used to measure the coefficient at 0.01 level of significance.

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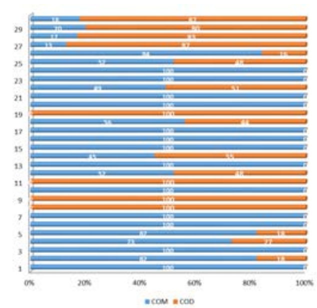
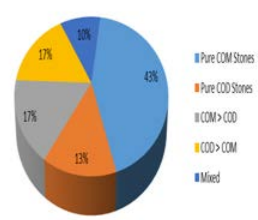
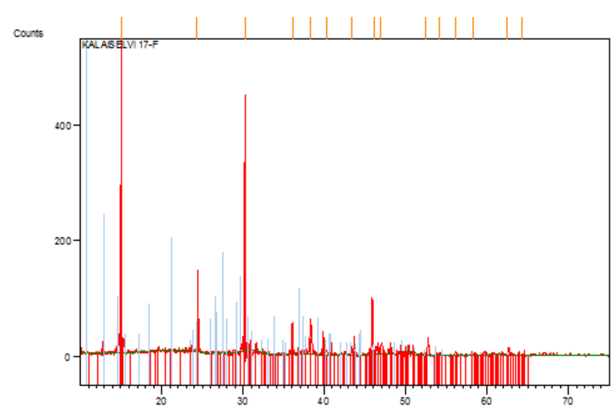


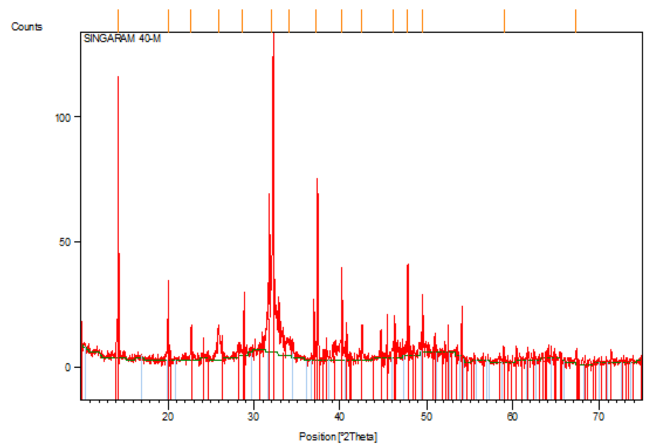


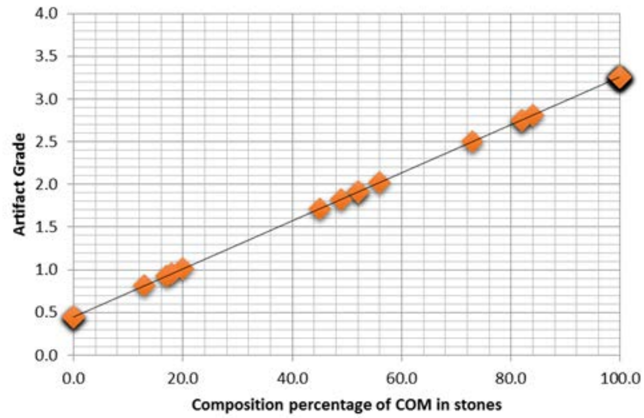
X-Ray Diffraction Spectroscopy

Spectroscopy Of A 100% Com Stone

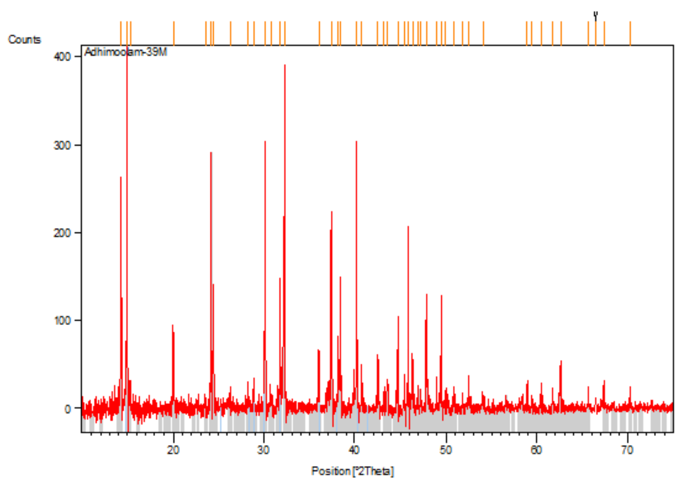


Spectroscopy of a 100% COD Stone





Spectroscopy of a Mixed Stone



Correlation of Imaging Appearance with Chemical Composition

	No of Stones	Mean Artifact Grade	Size
Pure COM Stones	13	3.5	15.1
Pure COD Stones	4	0.8	13.3
COM > COD	5	1.6	11.2
COD > COM	5	1.2	10.7
Mixed	3	1.0	14.7

Statistical Analysis of all the Characterisation data obtained from Sonographic and radiographic evaluation of nephrolithiasis were tested for correlation with the chemical character of the calculi. Pearson 2 tailed Correlation was used to measure the coefficient at 0.01 level of significance.

Twinkling	Sample Artifact Grade	Mean Size	Mean	COM	COD
0	1	0	100		
1	11	29.81	70.18		
2	4	57.75	42.25		
3	7	97.711	2.28		
4	7	100	0		

In particular, the grading of the twinkling artifact showed significant correlation (p-value 0.004) and was strongly associated with calcium oxalate monohydrate. In the stones that showed twinkling artifact of above 3, calcium oxalate monohydrate was found to predominate. Other factors such as homogeneity, comparative density, site and surface characteristics did not show any significant correlation with the chemical composition of the stones.

Summary	Measures
Null Deviance	39.42946569
Model Deviance	31.21468676
Improvement	8.214778932
p- Value	0.0042

Coefficient	StandardWald			
Regression	Coefficients		Error	Value
Constant-	0.000683957		17327434.18	-3.94725E-11
Grading of Twinkling Artifact	1.268282615	0.748813857	1.693722148	
COM	-0.040147616	173274.3418	-2.317E-07	
COD	-0.028248132	173274.3418	-1.63025E-07	

It was also observed that purely COD stones tended to be of smaller size.

Discussion

There is currently no reliable method in radio-diagnostics and clinical practice to determine the composition of urinary calculi before proposed therapy. There are many treatment options for urinary calculi and optimal treatment often depends on stone size, location and composition. Stone size and location may be determined by radiography before treatment. However, stone composition is difficult to determine unless the patient has a history of recurrent urolithiasis and even this history is often unlikely to be predictive of stone composition.

The treatment modalities available for upper tract urinary calculi include ESWL, percutaneous nephrolithotripsy, ureteroscopic manipulation and rarely open renal surgery. ESWL is often the first line therapeutic modality used but unfortunately it is not applicable to all stone compositions. For example, calcium oxalate dihydrate, uric acid and magnesium ammonium phosphate stones are usually successfully fragmented by ESWL whereas cystine, calcium oxalate monohydrate, calcium phosphate and urate stones are less likely to fragment using ESWL . Thus, many patients undergo ESWL therapy unsuccessfully due to the unknown composition of the stone. If one were able to determine stone composition before treatment, treatment failures and the need for re-treatment could be minimized or possibly even eliminated.

Multiple methods have been used in an attempt to determine stone composition preoperatively, including previous stone analysis, urinary pH , urine microscopy , plain x-ray,2 conventional CT , spiral CT , magnetic resonance imaging , and bone densitometry . Although some of these modalities appear promising, currently there is no definite available modality to determine stone composition before proposed therapy.

Twinkling effect & composition correlation

Our study shows that the twinkling artifact although not constant behind urinary stones, seems to strongly imply a relationship in vivo between the composition of stones and the presence of a twinkling artifact. This artifact appears in most cases when the composition of calculi is predominantly COM but also appears when it contains fractions of COD, but it is almost faint with pure COD stones. This observation agrees with that made by Rahmouni et al. , who showed that this artifact is generated by a random, strongly reflecting medium composed of individual reflectors.

Probably because of this relationship between the morphology and the composition of the stones, we also observed a correlation between the low grade of artifact and the predominant calcium oxalate dihydrate content of our stones.

Conclusion

Sonography combined with Radiography is an efficient and cost effective modality for diagnosis and evaluation of nephrolithiasis. Sonographic signs such as the Twinkling artifact which correlates well with predominance of COM in calculi can be useful in predicting the type of stone in vivo, which would be of assistance for the urologist in formulating further treatment strategy.

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