

Urolithiasis Diagnosis: The critical role of stone composition analysis for improved patient outcomes

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ABSTRACT

Urolithiasis is a common health problem worldwide, imposing a substantial clinical burden. The effective management of patients with renal stones relies heavily on accurate determination of stone composition. Stone analysis plays a pivotal role in guiding targeted treatment strategies, implementing appropriate preventive measures, and uncovering underlying metabolic or systemic abnormalities that contribute to stone formation and recurrence. The American Urological Association recommends that all patients with renal stones undergo at least one stone analysis prior to initiating treatment, with repeat analysis advised when a change in stone composition is clinically suspected. Advanced techniques like X-ray crystallography and infrared spectroscopy are recommended. Fourier Transform Infrared Spectroscopy (FTIR) is a superior semi-quantitative technique that provides detailed chemical composition information and distinguishes between surface and core stone compositions. Broader adoption of FTIR in Pakistan is necessary for enhancing treatment strategies for urolithiasis patients. This paper also covers the specimen collection process, transportation, and recommended analysis techniques to guide physicians treating urolithiasis patients.

Keywords: Urolithiasis, stone analysis, FTIR, infrared spectroscopy

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INTRODUCTION

Urolithiasis (renal stones) refers to the formation of stones in the kidney, ureter, urinary bladder, or urethra. Renal stones are one of the most painful urological conditions and are the third most common condition presenting to nephrology and urology clinics [1]. If appropriate dietary precautions or therapeutic interventions are not taken, there is more than a 50% chance of recurrence, which can adversely impact the patient's quality of life [2]. Renal stones cannot be attributed to a single element or component and may result from various risk factors, including an unhealthy diet, recurrent UTIs, metabolic disorders (such as type 2 diabetes, hyperuricemia, hyperparathyroidism, and obesity), poor hydration, decreased urine output, congenital birth defects (such as horseshoe kidney and medullary sponge kidney), anatomical obstructions in the urinary tract system, and geographic distribution (particularly hot climates) [2]. Renal stones typically occur between 20 and 60 years of age and are more prevalent in hot

climates, largely due to excessive sweating leading to dehydration. According to the NHANES (2007–2010) data estimated the prevalence of stones to be 10.6% in men and 7.1% in women [3]. Another study by Chen *et al.* reported an increasing trend in the prevalence of renal stones from 2007 to 2020 (8.9% to 9.9%) with significant increase in females during this period (6.5% to 9.1%) with no significant change in male prevalence [3]. South Asian countries have higher prevalence of renal stones and are referred to as the 'stone belt' of Asia [4-5]. Pakistan is an area where kidney stones are said to be extremely common. The prevalence of nephrolithiasis reported by Bibi *et al.*, varies from 7.4 per 100,000 in northern Pakistan to 200 per 100,000 in the southern part of the country, with males affected more than females by a ratio of 4:1 and more prevalent in the 21 to 40-year age group. They noted that calcium oxalate stones were the most common (80.1%) [5].

Understanding the pathophysiology and methods of stone analysis is important to enhance patient outcomes, reduce recurrence, and optimize healthcare resources in a region with a significant burden of renal stones. This issue is particularly significant in Pakistan, where the burden of urolithiasis is amplified by genetic predisposition, dietary habits, and environmental influences. Although clinicians may possess a general understanding of renal stone disease, limited awareness of specific stone subtypes, modern

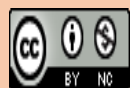
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analytical techniques, and individualized management approaches often result in suboptimal patient care. This article aims to bridge these knowledge gaps and provides stone-specific preventive strategies to improve clinical outcomes.

Renal stone formation occurs when minerals precipitate and crystallize in supersaturated urine containing lithogenic substances such as calcium, oxalate, uric acid, and cystine. These crystals adhere to the urothelial surface, creating a nidus that promotes progressive stone enlargement. Urinary pH plays a critical role in this process, as uric acid stones typically develop in acidic urine, whereas calcium phosphate and struvite stones are more commonly associated with alkaline urinary environments [6].

Crystal retention in the urinary tract system can lead to stone formation, particularly in the presence of anatomical defects like horseshoe kidney and medullary sponge kidney. Damage to the renal tubules can also create a nidus for crystal adhesion and growth. Urine stasis or retention may contribute to stone formation as well [6]. Additionally, genetic factors such as cystinuria and hypercalciuria, along with poor lifestyle choices and environmental factors, play crucial roles in the formation of renal stones.

Renal stones are categorized according to their composition. The different types of renal stones and their causes are detailed in Table-I. Various conditions can lead to differences in the composition of stones.

Once renal stones have been retrieved, along with analysing their composition, several additional parameters must be assessed. Firstly, X-ray imaging of the kidney, ureter, and urinary bladder to help determine the radiopacity of the stones, as calcium oxalate/phosphate/carbonate stones typically appear strongly radiopaque, while struvite and cystine stones are poorly radiopaque, and uric acid and xanthine stones are translucent [7].

Furthermore, a comprehensive urine analysis or urine detailed reported should be done, to identify crystals present in the urine; urine culture and sensitivity test should be conducted to detect any urinary tract infections, and urinary pH should be determined, as decreased urinary pH levels are associated with uric acid stones formation. Lastly, enzymes analysis or urine amino acid analysis may be necessary to evaluate a patient presenting with cystine or xanthine stones formation.

Specimen Collection and Transport: When collecting specimens for stone analysis, the source of the specimen is crucial for determining the appropriate treatment approach. Where possible,

whole stone should be collected, ensuring it is dry, clean and transported preferably at ambient temperature. Stones may partially dissolve if left in urine for prolonged periods. To avoid contamination or physical damage during transport, specimens should be placed in a clean, dry bag or a screw-capped plastic container. Proper adherence to recommended collection and transport protocols is essential to preserve specimen integrity and ensure reliable stone analysis. Inaccurate results may arise when stones are embedded within tissue, submitted in liquid-filled containers, or accompanied by excessive non-stone material.

Analysis of Stone Composition: Current recommendations favor advanced analytical techniques such as X-ray crystallography and Fourier Transform Infrared Spectroscopy (FTIR) over conventional chemical analysis for renal stone evaluation. These methods are non-destructive and provide high accuracy, sensitivity, and analytical efficiency. A key advantage is their ability to distinguish between the core and surface composition of a stone, an important consideration in clinical management, as the nidus may differ substantially from the outer layers and influence treatment and preventive strategies.

X-ray crystallography is regarded as the reference method for defining the exact crystalline structure of stone material; however, it requires relatively large, intact specimens and involves complex, time-intensive, and costly preparation. In contrast, FTIR offers comparable accuracy with greater practicality, as it is faster, more economical, and suitable for routine clinical use. Also, it is more sensitive to amorphous (non-crystalline) materials, which can be common in renal stones. Traditional chemical composition analysis methods for renal stone analysis are known to be less sensitive, more time taking, less accurate and more cumbersome compared to X-ray crystallography and FTIR.

In Pakistan, many laboratories still rely on traditional chemical composition analysis. Given the importance of accurate stone analysis in guiding treatment decisions for patients with urolithiasis, there is a need for broader adoption of advanced techniques like FTIR in laboratories across Pakistan.

A study by Khan *et al.* reported discrepancies between chemical analysis and FTIR in kidney stone evaluation. While both methods identified compositions such as calcium oxalate, uric acid, carbonate apatite, and magnesium ammonium phosphate hexahydrate, FTIR more frequently detected mixed stone compositions that were not

identified by chemical methods [7]. According to the American Urological Association Guidelines, it is recommended that patients with renal stones must have at least one stone analysis before initiation of the treatment [8-9]. A second analysis is indicated only if there is a suspicion of change in stone composition. As shown in Table-II, studies from different countries using various analytical methods, including Fourier Transform Infrared Spectroscopy (FTIR) and conventional chemical analysis consistently report calcium oxalate as the most common renal stone composition. While both methods identify calcium oxalate as the predominant stone type, FTIR provides more detailed and precise compositional characterization. In contrast, chemical analysis largely reports broader calcium-based stones, supporting the use of advanced techniques for accurate stone analysis.

Management and Prevention: The management of renal stones depends on their size, type, location, and associated symptoms. It can be categorized into medical treatment, lifestyle modifications, and surgical interventions.

Medical Treatment: This involves supportive and conservative management such as adequate hydration, pain management with analgesics or NSAIDs, and Medical Expulsive Therapy (MET) for distal ureteric stones. MET uses α -blockers (e.g., tamsulosin) to relax the ureter and aid in the passage of stones smaller than 10mm [17]. Dietary modifications, including appropriate restrictions and increased fluid consumption, are key lifestyle interventions in preventing recurrent renal stone formation [18-19]. Lifestyle modifications include dietary limitations, for example, patients with calcium oxalate stones need to avoid oxalate rich foods (shown in table-III). Preventive measures involve regular follow-ups and metabolic evaluations to treat underlying abnormalities and prevent recurrence. In cases of inherited metabolic disorders, enzyme replacement or gene therapy may be required [20]. Large-scale global real-world research on conservatively managed calculi shows that the overall stone passage rate is 52% for proximal ureteral stones, whereas distal stones have a passage rate of 83% [21-22]. Spontaneous stone passage rates vary by stone size: stones <5 mm have an 89% passage rate, those measuring 5–7 mm have a 49% passage rate, and stones >7 mm have a passage rate of 29% [23].

Surgical Interventions: For stones larger than 7mm that are unlikely to pass spontaneously itself, surgical procedures may be necessary [24]:

- **Extracorporeal Shock Wave Lithotripsy:** This non-invasive procedure breaks stones (usually those smaller than 20mm) into small fragments and is generally the method of choice for most renal stones.
- **Ureteroscopy (URS):** This procedure uses a ureteroscope to visualize and remove stones from the urinary tract.
 - **Percutaneous Nephrolithotomy (PCNL):** A minimally invasive procedure involving a small incision to remove large or complex kidney stones (typically those larger than 20mm). PCNL is effective for removing large, ESWL-resistant stones [25-26].
 - **Open Surgery:** Reserved for cases with anatomical abnormalities or when endourological attempts fail.

The composition of a stone can significantly impact its management, particularly its disintegration by lithotripsy and the subsequent elimination of fragments. Stones made of uric acid and calcium oxalate dihydrate have a better coefficient of fragmentation than those composed of calcium oxalate monohydrate and cystine. Hard stones, such as those made of cystine, calcium oxalate monohydrate, and brushite, poorly respond to ESWL, making PCNL a viable alternative for their removal. [26-27]

Treatment for Specific Stone Types: Calculi composed of materials other than calcium oxalate require distinct therapeutic and preventive strategies, which are detailed below.

- **Brushite or Dahllite:** Formed in slightly acidic to alkaline pH, often caused by UTIs or other metabolic disorders. These stones require urgent prevention due to their tendency to plug kidney tubules and injure kidney cells. Brushite stones are extremely hard and often resistant to ESWL, necessitating other treatment modalities such as chemical treatment or open surgery [26].
- **Uric Acid:** Formed in acidic pH environments, these stones are relatively easy to treat with alkaline supplements to increase urinary pH and prevent stone formation. Ammonium hydrogen urate stones, caused by UTIs or alkaline treatment for conditions like hyperuricosuria, require uricosuric drugs [27].
- **Genetic Stones (Cystine, Xanthine, 2,8-Dihydroxyadenine):** These stones occur due to enzyme deficiencies involved in the metabolism of these minerals. Treatment involves enzyme replacement therapy [28-29].

Table-I: Stone composition types, causes, management and preventive measures.

Type	Subtypes	Causes	Management	Dietary Prevention
Calcium oxalate	Calcium oxalate Monohydrate (Whewellite)	- Hyperoxaluria - Hypercalciuria - Hypocitraturia	Extracorporeal Shock Wave Lithotripsy (ESWL) for Whewellite	- Maintain good hydration - Moderate calcium intake.
	Calcium oxalate Dihydrate (Weddellite)	- Inherited metabolic disorder of oxalate - Low water intake or dehydration - High salt consumption	- Surgical removal for hard Whewellite stone - Enzymes replacement in inherited metabolic disorders - Increased fluid intake - Hydrochlorothiazide (for increased Ca) - Citrate supplementation - Pyridoxine	- Limit oxalate intake (green leafy vegetables, spinach, nuts, peanuts, wheat bran, black tea and chocolate) - Limit animal protein intake (meat, eggs, milk, cheese) - Encourage citrate rich food intake (increase urinary citrate levels which may aid in preventing the formation of calcium oxalates stones) - Limit oxalate beverages (tea and cocoa)
Ammonium hydrogen phosphate	Struvite	- UTI (urea splitting bacteria) - Malnutrition	- Surgery - Antibiotics - Increased fluid intake	- Reducing high phosphorus foods (processed foods, cheese, milk and meat products) - Encourage citrate rich foods intake (cranberries, plums, prunes)
Calcium Phosphate	Brushite, Dahllite	- Hyperparathyroidism, distal renal tubular acidosis (low urine pH) - UTI (Alkaline urine pH) - Other metabolic disorders	- ESWL for Dahllite - Brushite extremely hard stones resisting ESWL, may require chemolytic treatment or open surgery	- Reduce sodium intake. - Limit animal protein intake.
Uric Acid	Uricite, ammonium urate	- Diet high in protein - Gout - Alkaline urine pH - Bowel disease - Hyperuricosuria	- Urine alkalinization - Purine restriction - allopurinol	- Limit purine rich foods (red meat, organ meats, shellfish and certain types of fishlike mackerel and herring) - Moderate protein intake (red meat and opt for lean protein sources such as poultry, fish, tofu and legumes) - Limit alcohol - Limit high fructose foods (sugar beverages, sweets and processed foods)
Genetic stones	Cystine	Inherited cystinuria	- Cystine crystallization preventive drugs - High fluid intake >3L per day - Surgical removal for large cystine stones.	- Limit animal protein - Limit sodium - Limit oxalate (spinach, rhubarb, nuts and chocolate) - Increase alkaline diet/agent (alkalizing effect on urine pH can help prevent cystine e.g: potassium citrate, berries, citrus fruits, melons, leafy greens and cucumber)
	Xanthine	Inherited Xanthuria	- Purine restriction - High fluid intake	- Limit purine rich foods (organ meats such as liver and kidney) - Moderate protein intake - Limit oxalate - Limit alcohol
	2,8-dihydroxyadenine	Inherited metabolic disorder	- High fluid intake - Uricosuric drugs	- Low purine diet - Limiting certain vegetables (asparagus, spinach and mushroom) - Low Adenine foods (meats, fish and legumes)
Drugs Related Stones		Long term treatment with specific drug	- Stop the causative agent - High fluid intake	Change to another drug.

Table-II: Summary of Renal Stone Composition Reported in Different Studies Using Various Analytical Techniques

Study (Year)	Country	Method of Stone Analysis	Most Common Stone
Imran K <i>et al</i> [10]	Pakistan	Fourier Transformation Infrared Spectroscopy	Calcium Oxalate (76.9%)
Bibi A <i>et al</i> [11]	Pakistan	Fourier Transformation Infrared Spectroscopy	Calcium Oxalate (80.1%)
Bhat A <i>et al</i> [12]	India	Fourier Transformation Infrared Spectroscopy	Calcium oxalate (91.5%)
Pyakurel D <i>et al</i> [13]	Nepal	Fourier Transformation Infrared Spectroscopy	Calcium oxalate monohydrate in (41%)
Hareendra PP <i>et al</i> [14]	Srilanka	Chemical analysis	Calcium oxalate (86%)
Zhang D <i>et al</i> [15]	China	Fourier Transformation Infrared Spectroscopy	Calcium oxalate (88.9%)
Ochmański W <i>et al</i> [16]	Poland	Chemical analysis	Calcium (88.3%)

Table-III: Foods with high oxalate content

Foods	Servings	Oxalate content
Sweet potatoes	½ cup	120 mg
Beetroot	¼ cup	50 mg
Spinach	1 oz	30 mg
Rhubarb	¼ cup	120 mg
Almonds	1/8 cup	14 mg
Hazelnut	¼ cup	28 mg
Lentils, dried beans	½ cup	85 mg
Peanuts	¼ cup	28 mg
Pistachio	½ cup	56 mg
Sesame seeds	1 teaspoon	2.5 mg
Okra	½ cup	100 mg
Star fruit	1 oz	30 mg
Buckwheat	2 oz	60 mg
Wheat bran	1 oz	30 mg
Avocado	1 fruit	19 mg
Dates	1 date	24 mg
Oranges	1 orange	29 mg
Grapefruit	½ fruit	12 mg
Raspberries	1 cup	48 mg
Canned Pineapple	½ cup	24 mg
French fries	4 oz	51 mg
Cheeseburger	1 burger	13 mg
Pizza with cheese	2 slices	13 mg
Carrot juice	1 cup	27 mg
Hot Chocolate	1 cup	65 mg
Lemonade	8 oz	15 mg
Tomato juice	1 cup	14 mg
Brownies	1 oz	31 mg

Please note this list is not exhaustive.

CONCLUSION

Urolithiasis is frequently encountered in nephrology and urology practice and, when inadequately managed, can substantially affect patient well-being. Accurate identification of stone composition is essential for guiding diagnosis, selecting appropriate therapy, and reducing recurrence. Fourier Transform Infrared Spectroscopy (FTIR) is currently recommended for stone analysis due to its reliability and diagnostic precision. Adoption of contemporary analytical techniques can markedly enhance the quality of stone evaluation and translate into improved clinical outcomes. Increasing awareness among healthcare professionals, along with investment in laboratory infrastructure and staff

training, represents an important step toward optimizing renal stone management.

CONFLICT OF INTEREST

None

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Declared none

AUTHORS' CONTRIBUTION

Syed Bilal Hashmi: Manuscript writing critically reviewed the intellectual content, final approval, accountable for all aspects of publication.

Halima Sarwar: Literature search and wrote initial manuscript, accountable for all aspects of publication.

Noreen Younus: Manuscript writing critically reviewed the intellectual content, final approval, accountable for all aspects of publication.

Maira Khalid: Manuscript writing critically reviewed the intellectual content, final approval, accountable for all aspects of publication.

Hafsa Majid: Manuscript writing, critically reviewed the intellectual content, final approval, accountable for all aspects of publication.

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