Chirurgia (2025) 120: 677-684
No. 6, November - December
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http://dx.doi.org/10.21614/chirurgia.3162

Kidney Anatomy, Stone Type: Is There a Link?

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Abbreviations:
FTIR: Fourier-transform infrared;
HSK: Horseshoe kidney;
URS: Ureteroscopy;
PCNL: Percutaneous nephrolithotomy;
CaOx: Calcium oxalate;
EAU: European Association of Urology.

Rezumat

Anatomia renală și tipul de calcul: există o legătură?

Introducere: Anomaliile anatomice renale sunt asociate cu alterarea drenajului urinar şi a pH-ului, factori care pot influența formarea şi compoziția calculilor urinari. Totuşi, puține studii au evaluat diferențele de compoziție a calculilor la pacienții cu anatomie renală anormală comparativ cu cei cu rinichi normal constituiți.
Metode: Studiul observațional a inclus 100 de pacienți tratați între septembrie 2023 şi august 2024 într-un centru universitar din sudul României. Compoziția calculilor a fost analizată prin spectroscopie în infraroşu cu Transformată Fourier (FTIR) şi clasificată în cinci tipuri principale. Au fost efectuate analize comparative şi multivariate pentru a evalua asocierile dintre morfologia renală, comorbidități şi tipul de calcul.
Rezultate: Calculii de acid uric (39%) şi oxalat de calciu (32%) au fost cei mai frecvenți. Pacienții cu rinichi în potcoavă şi rinichi ectopici au prezentat proporții mai mari de calculi de fosfat de calciu. Diabetul şi hiperuricemia au fost predictori semnificativi pentru calculii de fosfat de calciu, respectiv de acid uric. Nu s-a evidențiat o asociere statistic semnificativă între anatomia renală şi compoziția calculilor, deşi s-au observat diferențe descriptive.
Concluzii: Deşi anomaliile anatomice nu au demonstrat diferențe semnificative statistic în compoziția calculilor, factorii metabolici precum diabetul şi hiperuricemia au influențat semnificativ tipul de calcul. Analiza spectroscopică rămâne esențială pentru ghidarea managementului individualizat al litiazei renale

Cuvinte cheie: malformații renale, compoziția calculilor renali, spectroscopie FTIR, factori metabolici, litiază renală

Abstract

Background: Renal anatomical anomalies are associated with altered urinary drainage and pH, which may influence urinary stone formation and composition. However, limited studies have assessed the stone composition differences in patients with abnormal versus normal renal anatomy.

Received: 04.06.2025
Accepted: 16.07.2025

Methods: This observational study included 100 patients treated between September 2023 and August 2024 in a tertiary academic center in southern Romania. Stone composition was assessed using Fourier-transform infrared spectroscopy and categorized into five major types. Comparative and multivariate analyses were performed to assess associations between renal morphology, comorbidities, and stone type.
Results: Uric acid (39%) and calcium oxalate (32%) were the most common stone types. Patients with horseshoe kidney and ectopic kidneys showed higher proportions of calcium phosphate stones. Diabetes and hyperuricemia were significant predictors of calcium phosphate and uric acid stones, respectively. No statistically significant association was found between renal anatomy and stone composition, though descriptive differences were observed.
Conclusions: While anatomical anomalies did not show statistically significant differences in stone composition, metabolic factors such as diabetes and hyperuricemia strongly influenced stone type. Spectroscopic analysis remains essential in guiding individualized nephrolithiasis management.

Keywords: renal malformations, kidney stone composition, FTIR spectroscopy, metabolic factors, nephrolithiasis

Introduction

Renal stone disease is a prevalent and multifactorial condition (1) affecting a significant proportion of the population globally (2). Anatomical anomalies, dietary choices, and metabolic abnormalities are some of the factors that influence the composition of kidney stones (3). The potential of renal malformations, such as horseshoe kidney (HSK), ectopic kidney, and malrotated kidney, to disrupt normal urinary drainage can lead to stasis, recurrent infections, and altered urinary pH-factors that significantly influence the formation and composition of renal lithiasis (4). Calcium oxalate and uric acid stones are the most commonly reported types in the general population (5); however, anatomical abnormalities can lead to different distributions, with a higher prevalence of uric acid or infection-related stones such as struvite (6). Despite these clinical observations, comparative studies on the specific impact of renal malformations on stone composition remain limited.

This study aims to conduct a spectroscopic analysis of kidney stone composition in patients with renal anomalies, compared to those with normal renal anatomy.

The objective is to assess the incidence of different stone compositions, examine statistical correlations between renal morphology and stone types, and identify the metabolic or anatomical mechanisms responsible for changes in stone composition.

Materials and Methods

Study Population

This is a retrospective observational study that analyzed patient data collected between September 1, 2023, and August 31, 2024, at a tertiary care academic urology center in southern Romania. We included patients aged 18 years and older who had confirmed upper urinary tract stones, identified either through spontaneous passage or retrieved during procedures such as percutaneous nephrolithotomy (PCNL), ureteroscopy (URS), or laparoscopic surgery. Patients were excluded if they presented with isolated bladder or urethral stones, if their clinical data were incomplete, or if stone composition analysis could not be performed. Data obtained included demographic variables, body mass index, urine pH, and medical history concerning diabetes mellitus, hypertension, hyperlipidemia and hyperuricemia. Medical history was determined through medical records, patient self-reports, or verification of chronic medication use. Self-reported information also covered alcohol and tobacco consumption.

Stone Composition Grouping

The composition of the stones was analyzed using a Fourier-transform infrared (FTIR) spectrometer. Stone compositions were categorized into five groups following the recommendations of the European Urological Association and the Mayo Clinic classification: (1) groups containing more than 50% calcium oxalate (CaOx); (2) groups containing more than 50% uric acid, uric acid dihydrate, or sodium; (3) groups containing any amount of cystine; (4) groups characterized by infection stones (>10% struvite or ammonium acid urate); and (5) groups containing more than 50% tricalcium phosphate, brushite, or carbapatite.

Statistical Analysis

The study comprised 100 patients, divided into two groups based on renal morphology: patients with kidney anomalies (such as HSK, ectopic kidney, or malrotated kidney) and those with normal renal anatomy, who served as the control group. Patients with only bladder or urethral stones were excluded from the study. The statistical analysis was conducted out using IBM SPSS Statistics version 26®, which includes descriptive statistics, comparative analysis (Chi-square and t-tests), and logistic regression. A significance level of $p < 0.05$ was set.

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional ethics review board. All patient data were anonymized to maintain confidentiality and ensure compliance with data protection regulations.

Results

There were 100 patients in the study with complete data, of which 55 were male. The mean age of the patients was 50.20 years, with a range of 18-82 years. However, the difference between the mean age of males (48.80 years) and females (51.91 years) was not statistically significant ($p = 0.417$). In terms of comorbidities, the most frequent were hyperlipidemia (55%), followed by diabetes mellitus (43%), hyperuricemia (25%), hypertension (24%), and urinary tract infections (25%).

Stone Composition

The quantitative analysis revealed an average stone count of 2.65 per patient, ranging from 1 to 4, and a mean stone size of 17.67 mm. The compositional study revealed that uric acid stones were the most common (39%), followed by calcium oxalate (32%), and calcium phosphate stones (20%). Cystine (6%) and struvite stones (3%) were among the less common components. *Fig. 1* show the macroscopic and microscopic appearance of uric acid and calcium oxalate stones, illustrating their distinct surface characteristics.

Gender-specific patterns revealed that males had a greater incidence of uric acid stones (41.8%) and calcium oxalate stones (34.5%), whereas females had a higher prevalence of calcium phosphate (24.4%) and cystine stones (8.9%). However, statistical testing indicated no significant association between sex and stone composition [$\chi^2(4) = 2.607$, $p = 0.625$].

Underlying Comorbidities

There were notable correlations found between the composition of stones and specific comorbidities. Hyperuricemia was highly associated with uric acid stones ($p=0.006$), while diabetes mellitus was strongly related to calcium phosphate stones ($p = 0.021$). Calcium phosphate and struvite stones were both influenced by urinary tract infections ($p = 0.038$), with the latter highlighting its well-established link to infection-related lithogenesis, as shown in *Table 1*.

On the other hand, there were no significant correlations found between stone composition and hypertension ($\chi^2(4) = 1.775$, $p = 0.777$), hyperlipidemia ($\chi^2(4) = 4.486$, $p = 0.344$), or family history ($\chi^2(4) = 0.844$, $p = 0.933$), suggesting that these variables may not have a direct impact on stone type.

Age and Stone Composition

The association between age and urinary stone types was investigated by grouping patients into seven age groups, as shown in *Table 2*. Stone composition was examined within these age groups and further classified by kidney anatomy, which included normal anatomy, HSK, ectopic kidney, and malrotated kidney. Although there was no statistically significant association between age groups and stone composition ($p = 0.440$), descriptive patterns have been identified.

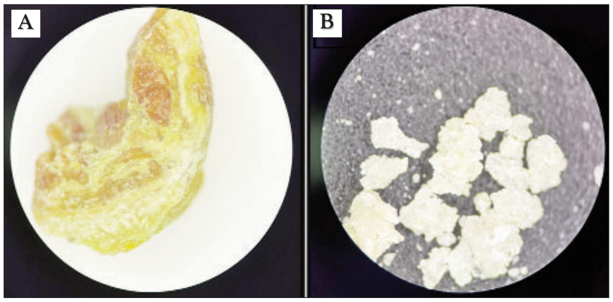

Figure 1. **(A)** Bright-field observation of uric acid kidney stones, highlighting their amber to orange-brown coloration, relatively smooth surfaces, and subtle layered architecture.
(B) Microscopic images of calcium oxalate renal calculi, revealing translucent, pale-yellow crystalline aggregates with irregular, granular surfaces under bright-field illumination.

Table 1. Association of clinical variables with primary stone composition.

Variable	Calcium oxalate (n)	Uric acid (n)	Cystine (n)	Struvite (n)	Calcium phosphate (n)	Total (n)	p-value
Hypertension							0.777
- Yes	7	11	2	1	3	24	
- No	25	28	4	2	17	76	
Diabetes mellitus							0.021
- Yes	13	11	3	3	13	43	
- No	19	28	3	0	7	57	
Hyperlipidemia							0.344
- Yes	20	17	4	1	13	55	
- No	12	22	2	2	7	45	
Hyperuricemia							0.006
- Yes	2	17	2	1	3	25	
- No	30	22	4	2	17	75	
Urinary infection							0.038
- Yes	6	8	0	2	9	25	
- No	26	31	6	1	11	75	
Family history							0.933
- Yes	11	12	1	1	7	32	
- No	21	27	5	2	13	68	

Table 2. Stone composition by age group.

Age group (years)	Calcium oxalate (%)	Uric acid (%)	Cystine (%)	Struvite (%)	Calcium phosphate (%)	Total (n)
18-27	41.2	35.3	5.9	0.0	17.6	17
28-37	36.4	54.5	9.1	0.0	0.0	11
38-47	27.8	50.0	5.6	5.6	11.1	18
48-57	20.0	33.3	6.7	6.7	33.3	15
58-67	33.3	40.0	0.0	0.0	26.7	15
68-75	46.2	23.1	7.7	0.0	23.1	13
75-82	18.2	36.4	9.1	9.1	27.3	11

As illustrated in *Figs. 2, 3*, calcium oxalate stones were most common in the elderly, particularly those aged 68 to 75 years, accounting for 46.2% of cases. Uric acid stones were more common in younger age groups, particularly those aged 28-37 and 38-47 years, whereas calcium phosphate stones were most common in middle-aged patients, particularly those aged 48-57 years, which corresponded to a higher incidence of metabolic conditions such as diabetes mellitus in this population.

The univariate analysis assessed the influence of age group and kidney anatomy on the type of

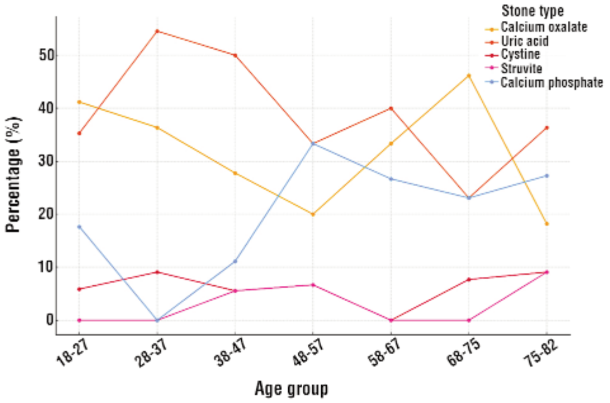

Figure 2. Distribution of stone types across age groups.

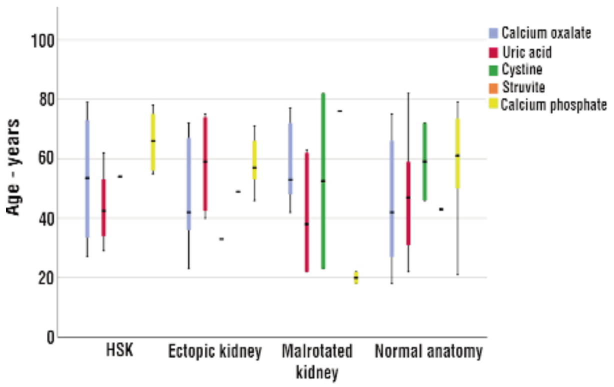

Figure 3. Stone composition in relation to age and kidney anatomy.

primary stone composition. The data demonstrated no statistically significant effect of age group [F(6,92) = 1.058, p=0.394] or kidney anatomy [F(1,92) = 1.713, p=0.194] on stone composition. With a significant intercept [F(1,92) = 50.331, $p < 0.001$] and low explanatory power (R2 = 0.086, adjusted R2 = 0.017), the model's findings suggest that neither age group as well as anatomical features are significant predictors of stone composition in this cohort.

Kidney Anatomy and Stone Composition

The association between kidney anatomy and urinary stone composition was explored by dividing patients into four anatomical subgroups: normal anatomy, HSK, ectopic kidney, and malrotated kidney. Across all groups, uric acid stones were the most prevalent, followed by calcium oxalate and calcium phosphate stones, as represented in *Fig. 4*. However, specific tendencies were detected based on anatomical variances. In patients with normal renal anatomy, a higher prevalence of uric acid stones (42%) and calcium oxalate stones (36%) was observed, reflecting the distribution typically seen in the general population.

In contrast, patients with HSKs, revealed a similarly high incidence of uric acid stones (44.4%) but a considerably enhanced occurrence of calcium phosphate stones (27.8%). Ectopic kidneys revealed a reasonably even distribution of calcium oxalate (31.3%) and calcium phosphate stones (31.3%), with uric acid stones being significantly less frequent (25%). Patients with malrotated kidneys showed a distinct distribution of stone types in our cohort, with uric acid stones accounting for 37.5% and an unexpectedly high proportion of cystine stones at 12.5%. Although these figures are noteworthy, the small number of cases in this subgroup limits the ability to draw firm conclusions. As such, these observations should be seen as preliminary and interpreted with caution, particularly in the absence of statistical significance.

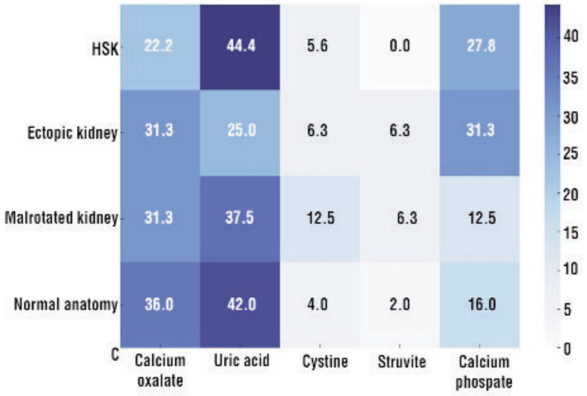

Figure 4. Heatmap of stone composition by kidney anatomy.

Despite these descriptive variations, statistical analysis did not demonstrate a significant link between kidney anatomy and stone composition [$\chi^2(12) = 7.567$, p = 0.818].

Predictors of Stone Composition

Multinomial logistic regression analysis identified significant predictors of stone composition, as detailed in *Table 3*. Diabetes mellitus emerged as a significant predictor of calcium phosphate stones (p = 0.039), while hyperuricemia substantially increased the likelihood of uric acid stones (p = 0.030). Urinary infections were associated with higher odds of both calcium oxalate (p = 0.026) and uric acid stones (p = 0.050).

The model demonstrates moderate explanatory power, with pseudo R-squared values ranging from 18.7% (McFadden) to 42.1% (Nagelkerke). However, instability was noted in predicting rare stone types, such as struvite, likely due to limited data availability and potential multicollinearity among the predictors.

Discussion

This study presents an inquiry into the composition of urinary stones in patients from southern Romania, applying FTIR spectroscopy for exact categorization and analysis. Supported by the EAU and AUA, routine stone composition analysis offers vital insights into the metabolic and environmental factors behind stone formation, paving the way for targeted prevention and treatment strategies (7).

Two basic procedures are available for stone analysis: the chemical spot test and FTIR spectroscopy (8). While chemical approaches are still extensively employed because to their simplicity and cost-effectiveness (9), they often offer only approximate information regarding the basic structure of mixed stones. These approaches have considerable drawbacks, including subjectivity in interpreting results (10), inability to detect rare or unidentified elements, and the requirement for relatively large sample volumes (10-15 mg), which

Table 3. Multivariate and univariate logistic regression analysis of predictors for stone composition.

Predictor	Stone type	B	SE	Wald	OR (Exp(B))	95% CI for Exp(B)	p-Value
Age (years)							
Calcium oxalate	-0.016	0.021	0.539	0.984	0.944 – 1.027	0.463	
Uric acid	-0.021	0.021	1.003	0.979	0.940 – 1.020	0.317	
Cystine	-0.016	0.032	0.249	0.984	0.924 – 1.048	0.618	
Struvite	-0.074	0.061	1.457	0.929	0.823 – 1.047	0.227	
Hypertension							
Calcium oxalate	-0.563	0.831	0.459	0.569	0.112 – 2.902	0.498	
Uric acid	-0.662	0.847	0.612	0.516	0.098 – 2.712	0.434	
Cystine	-0.903	1.154	0.612	0.405	0.042 – 3.894	0.434	
Struvite	-0.371	1.552	0.057	0.690	0.033 – 14.444	0.811	
Diabetes mellitus							
Calcium oxalate	0.720	0.788	0.835	2.055	0.438 – 9.633	0.361	
Uric acid	1.652	0.799	4.282	5.220	1.091 – 24.968	0.039	
Cystine	0.748	1.188	0.396	2.113	0.206 – 21.708	0.529	
Struvite	-17.381	1676.866	0.000	2.83E-8	-	0.992	
Hyperuricemia							
Calcium oxalate	0.929	1.008	0.848	2.532	0.351 – 18.270	0.357	
Uric acid	-1.787	0.824	4.706	0.167	0.033 – 0.842	0.030	
Cystine	-0.931	1.156	0.648	0.394	0.041 – 3.801	0.421	
Struvite	-2.068	1.986	1.084	0.126	0.003 – 6.200	0.298	
Urinary infection							
Calcium oxalate	1.550	0.697	4.942	4.711	1.201 – 18.474	0.026	
Uric acid	1.437	0.732	3.850	4.207	1.002 – 17.670	0.050	
Cystine	17.591	0.000	-	4.36E7	-	-	
Struvite	-2.191	2.258	0.942	0.112	0.001 – 9.337	0.332	
Hyperlipidemia							
Calcium oxalate	0.362	0.672	0.291	1.437	0.385 – 5.365	0.590	
Uric acid	1.015	0.681	2.220	2.759	0.726 – 10.482	0.136	
Cystine	0.359	1.058	0.115	1.432	0.180 – 11.387	0.734	
Struvite	0.594	1.597	0.138	1.811	0.079 – 41.406	0.710	
Family history							
Calcium oxalate	-0.319	0.689	0.214	0.727	0.189 – 2.803	0.643	
Uric acid	-0.059	0.714	0.007	0.943	0.232 – 3.824	0.934	
Cystine	0.418	1.293	0.105	1.519	0.121 – 19.134	0.746	
Struvite	0.665	1.611	0.170	1.944	0.083 – 45.715	0.680	

can be difficult when evaluating small stones (11).

Alternatively, FTIR spectroscopy offers a more sophisticated option, characterized by lower cost of operation, partial automation, quick analysis (12), and the ability to recognize organic and non-crystalline substances (13).

This research highlights descriptive patterns suggesting a possible relationship between renal structural differences and stone composition. However, given the lack of statistical significance, these findings should be interpreted with caution and regarded as preliminary hypotheses that warrant further investigation in larger, prospective cohorts.

Patients with normal renal architecture had stone compositions similar with earlier findings (14), which were uric acid (42%) and calcium oxalate (36%) stones, assessing the theory that metabolic processes are the primary determinants of stone formation in structurally normal kidneys.

In our cohort, patients with HSKs demonstrated a stone composition pattern characterized by relatively high proportions of uric acid (44.4%) and calcium phosphate stones (27.8%). Although these differences did not reach statistical significance, they are in line with previously published data, suggesting that such patterns may be consistent in this subgroup. However, given the limited sample size and reduced statistical power, these findings should be interpreted with caution and considered as hypothesis-generating rather than conclusive (15). The increased incidence of calcium phosphate stones may be linked to urinary stasis and impaired drainage, hallmark features of HSK, which promote an alkaline urinary environment conducive to calcium phosphate crystallization (16). Conversely, the elevated proportion of uric acid stones might reflect a combination of metabolic factors, such as hyperuricosuria or intermittent urine acidification, which can occur in these patients despite the anatomical abnormalities (16). Additionally, metabolic disorders typically linked with HSK - such as hyperparathyroidism, hypercalciuria, and hypocitraturia - further increase the risk of stone development (17).

In comparison, patients with ectopic kidneys revealed a more balanced distribution of stone types, with calcium oxalate 31.3% and uric acid stones accounting for 25%.

Sex-related variations were also identified, with a male-to-female ratio of 1.22:1. Males had a higher frequency of calcium oxalate and uric acid stones, likely explained by increasing testosterone levels and lower urine pH (18). In contrast, females showed a larger proportion of calcium phosphate stones, perhaps due to anatomical vulnerability to urinary tract infections and their connection with alkaline urine (19).

Age-related tendencies further confirmed recent findings, suggesting a decreasing frequency of calcium oxalate stones with advancing age. Comorbidity study found high prevalence of diseases such as hyperlipidemia (55%), diabetes mellitus (43%), and chronic renal disease (49%), all of which significantly impact stone development. Specifically, diabetes mellitus has been associated with a higher incidence of calcium phosphate stones, while hyperuricemia was considerably linked to uric acid stone formation.

Multivariate analysis identified diabetes, hyperuricemia, and urinary infections as significant predictors of stone composition, highlighting the importance of incorporating metabolic examinations into routine clinical practice. Recent experimental findings also highlight the role of oxidative stress, metabolic imbalance, and cellular responses, mechanisms that may affect the renal microenvironment and disease development even in nonmalignant settings (20).

Clinically, these findings show the necessity of a multidisciplinary approach to kidney stone treatment, integrating the knowledge of endocrinologists, nephrologists, and dietitians. Prevention efforts should prioritize metabolic management, hydration optimization, and dietary changes. Anatomical anomalies, despite not significantly affecting stone composition, require specialized surgical planning and imaging.

Despite its contributions, the study has limitations. The sample size, while sufficient for descriptive research, may lack the ability to identify subtle relationships. The cross-sectional design excludes causal inferences, and the absence of data on diets, hydration intake, genetic variables, and biochemical markers limits the depth of study. Additionally, self-reported comorbidities may induce recall bias, especially in retrospective circumstances.

Beyond anatomical considerations, recent literature increasingly emphasizes the need to interpret stone formation through a broader biochemical and epidemiological lens. This perspective aligns with our findings and supports the importance of advanced analytical techniques in uncovering clinically relevant compositional patterns.

Emerging evidence from large-scale cohort studies reinforces the importance of compositional heterogeneity in kidney stones. A recent German investigation analyzing over 42,000 stones found that more than half exhibited mixed composition, with calcium oxalate-phosphate combinations accounting for 33.8%, while uric acid stones made up only 7.6% of cases. These results illustrate the biochemical complexity of stone formation and highlight the clinical utility of FTIR spectroscopy in detecting even minor stone constituents - details that are often missed by conventional chemical analysis methods (21).

A regional study conducted in Austria analyzed over 300 kidney stones using FTIR spectroscopy and found that calcium oxalate was the most commonly identified component, followed by calcium phosphate, uric acid, struvite, and cystine. This pattern aligns well with global epidemiologic data and further supports the value of FTIR as a diagnostic standard. Its ability to accurately detect both crystalline and amorphous phases makes it especially useful in identifying mixed stones or rare compositions that might be overlooked by more traditional chemical methods (22).

Our observations in patients with horseshoe kidneys are in line with findings from a recent meta-analysis, which reported a 36% prevalence of nephrolithiasis among adults with this anomaly. Most stones in that group were calcium-based - specifically calcium oxalate (64.2%) and calcium phosphate (18.8%) - while uric acid stones were relatively uncommon, at just 3.8%. This distribution is comparable to what we noted in our cohort and may reflect the distinct urodynamic environment associated with HSK, where impaired drainage and urinary stasis could promote the formation of certain stone types (23).

Recent clinical data also point to the strong influence of systemic metabolic conditions on stone composition. For example, individuals with diabetes appear more prone to forming uric acid and calcium phosphate stones, likely due to chronic changes in urinary pH and solute handling. Similarly, patients with hyperuricemia or gout often develop uric acid stones as a direct consequence of elevated uric acid levels. These associations are consistent with our multivariate analysis, which identified diabetes, hyperuricemia, and urinary infections as independent predictors of stone type. Taken together, these findings support a more integrated clinical approach that addresses metabolic factors alongside anatomical considerations (24).

Conclusion

This study analyzed kidney stone composition in patients with renal malformations, revealing that uric acid and calcium phosphate stones were notably prevalent. While anatomical anomalies such as horseshoe and malrotated kidneys showed distinct compositional trends, only metabolic factors - especially hyperuricemia, diabetes, and urinary infections - were statistically associated with stone type. These findings highlight the importance of FTIR spectroscopy and metabolic assessment in managing stone disease in anatomically abnormal kidneys.

Conflicts of Interest

This research was financially supported by the Academy of Romanian Scientists (AOSR) -Ilfov 3, 050044, Bucharest, Romania.

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