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Prevalence and Clinical Significance of Monogenic Gene Mutations in High-Risk Patients With Urolithiasis: A Prospective Cross-Sectional Next-Generation Sequencing Study

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Abstract

Monogenic disorders affecting renal tubular transport and metabolic pathways are increasingly recognized as important contributors to urolithiasis. However, the prevalence and clinical significance of such mutations in mixed-risk populations remain incompletely defined. We aimed to investigate the prevalence of monogenic gene mutations associated with urolithiasis and evaluate their clinical associations in patients stratified by risk features. This prospective cross-sectional observational study included 143 patients with radiologically confirmed urolithiasis who underwent whole blood next-generation sequencing (NGS) testing targeting 47 genes associated with hereditary or metabolic stone disorders. Patients were classified into high-risk (n = 75) and low-risk (n = 68) groups. High-risk patients included patients with recurrent stone formation, early age at onset, or a family history of urolithiasis. Low-risk patients consisted of individuals with incidental urolithiasis during nephrological evaluation. Clinical, metabolic, and NGS features were compared between groups. Logistic regression analysis was performed to identify factors associated with high-confidence monogenic mutations. High-risk patients had significantly earlier onset of urolithiasis and higher prevalence of hypercalciuria and overall gene mutations compared to the low-risk group. High-confidence pathogenic gene mutations were detected in 57 patients (39.9%), again more frequently among high-risk individuals ($p < 0.001$). Multivariate logistic regression identified recurrent stone formation as an independent factor associated with high-confidence monogenic mutations ($p < 0.001$). Monogenic gene mutations associated with renal stone disease are common among patients with high-risk clinical features, particularly recurrent stone formation and early onset. These findings support the implementation of targeted genetic testing in selected high-risk patients to guide preventive strategies and personalized management.

1. Introduction

Urolithiasis is a common urological disorder with a lifetime prevalence of 10–15% worldwide [1]. The disease imposes substantial healthcare burden due to its recurrent nature, potential complications including chronic kidney disease, and the need for repeated surgical interventions [2]. Although environmental factors and metabolic abnormalities play major roles in stone formation, an increasing body of evidence suggests that genetic predisposition contributes significantly to its pathogenesis [3–5].

In recent years, advances in genomic technologies have enabled the identification of numerous monogenic disorders associated with urolithiasis [6, 7]. Mutations affecting renal tubular transport, mineral metabolism, and metabolic pathways can lead to imbalances in urinary solute composition and subsequent stone formation [8]. Examples include genes involved in oxalate metabolism, calcium transport, renal tubular acidosis, and cystine transport [9]. These disorders represent a clinically important but often underrecognized cause of urolithiasis. Previous genetic studies have focused on pediatric populations and were largely case-based [10–12]. In such populations, monogenic causes have been reported in up to 15–30% of cases depending on the cohort and diagnostic approach [13]. These findings highlight the importance of considering genetic etiologies, particularly in patients with early-

onset, recurrent disease, or family history. However, the prevalence and clinical significance of monogenic mutations in broader patient populations remain unclear.

Next-generation sequencing (NGS) has emerged as a powerful tool for identifying genetic causes of urolithiasis. Targeted sequencing panels may enable clinicians to detect monogenic disorders that disrupt renal tubular transport and metabolic pathways involved in stone formation [14–16]. Identification of such genetic abnormalities may help earlier diagnosis of underlying metabolic conditions, enable personalized preventive strategies, and provide information for family counseling. Despite these advances, genetic testing is not yet routinely utilized in everyday clinical practice. One major challenge is the limited evidence regarding which patient populations are most likely to benefit from genetic screening. Identifying this subgroup of patients could help guide a risk-stratified approach to genetic testing and improve the clinical utility of genomic evaluation in patients with urolithiasis.

Our study aimed to investigate the prevalence of monogenic gene mutations in patients with urolithiasis using a targeted NGS panel consisted of 47 genes associated with hereditary or metabolic stone disorders. Based on the hypothesis that patients with high-risk features, defined as recurrent stone formation, early onset, or presence of a family history, would demonstrate a higher prevalence of monogenic mutations, we further evaluated the association between clinical features and high-confidence pathogenic gene variants.

2. Materials and Methods

2.1. Study design and patient population

This study was designed as a prospective cross-sectional observational study conducted at Gangnam Severance Hospital between August 2022 and November 2025. Patients with radiologically confirmed urolithiasis who underwent genetic testing as part of clinical evaluation were included.

Patients were stratified into two groups according to predefined risk criteria. The high-risk group consisted of patients who met at least one of the following criteria: recurrent stone formation, early age at onset (< 40 years), and a family history. The low-risk group included patients who were incidentally diagnosed with urolithiasis during nephrological evaluation and did not meet high-risk criteria.

This study was approved by the institutional ethics committee of Gangnam Severance Hospital (2019-0838-001) after reviewing the protocols employed. All study procedures complied with the principles of the 1946 Declaration of Helsinki and its 2008 update. All patients provided consent peripheral blood samples for genetic testing using NGS.

2.2. Genetic testing

Whole blood samples were analyzed using a targeted NGS panel comprising 47 genes associated with renal stone disease and metabolic disorders affecting urinary stone formation. The panel included both

well-established monogenic causes and candidate susceptibility genes, selected based on prior evidence in the literature [1].

According to the American College of Medical Genetics and Genomics (ACMG) guidelines, variants were categorized into two major groups: high-confidence monogenic stone genes, defined as genes with definitive or strong evidence linking them to hereditary nephrolithiasis or nephrocalcinosis; and risk-modifier genes, including genes associated with increased susceptibility to stone formation but not considered definitive monogenic causes [14]. The complete list of genes and their associated phenotypes is presented in Supplementary Table 1.

2.3. Clinical and laboratory evaluation

Clinical data were collected from electronic medical records and included: age, gender, body mass index, comorbidities, and family history of urolithiasis. Laboratory evaluation included serum chemistry and urine metabolic analysis. Metabolic abnormalities were defined according to standard diagnostic thresholds and included hypercalciuria, hyperoxaluria, hypercalcemia, hyperparathyroidism, and proteinuria.

2.4. Stone composition analysis

Stone composition analysis was available for all patients in the high-risk group who underwent surgery. Stone composition analyses were performed using Fournier-transform infrared spectrometry (Green Cross Laboratories, Yongin, South Korea).

2.5. Statistical analysis

Continuous variables were presented as median with interquartile range, and categorical variables were reported as frequencies and percentages. Comparisons between high-risk and low-risk groups were performed using appropriate statistical tests. Logistic regression analysis was performed to identify factors associated with high-confidence monogenic gene mutations. Variables with clinical relevance were included in the model. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Baseline clinical characteristics

A total of 143 patients were included in the study, consisting of 75 (52.4%) high-risk and 68 (47.6%) low-risk patients. The median age of the overall cohort was 45 (IQR 27.0–56.0) years. High-risk patients had significantly earlier age at onset compared with low-risk patients. Hypertension was more common among high-risk patients (40.0% vs. 14.7%, p < 0.001), whereas the prevalence of other comorbidities was similar between groups (Table 1).

Table 1
Baseline clinical characteristics.

N	Overall	High-risk	Low-risk	*p*
	143.0	**75.0**	**68.0**	
Age, years	45.0 (27.0–56.0)	41.0 (31.0–63.5)	49.0 (41.0–57.0)	*< 0.001*
Gender				*0.094*
Male	86 (60.1%)	53 (70.7%)	33 (48.5%)	
Female	57 (39.9%)	22 (29.3%)	35 (51.5%)	
BMI (kg/m2)	25.9 (23.2–27.9)	25.5 (22.9–27.5)	26.4 (24.0–28.3)	*0.544*
Family history, n (%)	17 (11.9%)	12 (16.0%)	5 (7.4%)	*0.506*
Comorbidities				
Chronic kidney disease	13 (9.1%)	4 (5.3%)	9 (13.2%)	*0.067*
Hypertension	40 (28.0%)	30 (40.0%)	10 (14.7%)	*< 0.001*
Diabetes mellitus	38 (26.6%)	25 (33.3%)	13 (19.1%)	*0.064*
Nephritis / nephropathy	13 (9.1%)	7 (9.3%)	6 (8.8%)	*0.975*
Coronary heart disease	4 (2.8%)	3 (4.0%)	1 (1.5%)	*0.395*
Crohn's disease	4 (2.8%)	2 (2.7%)	2 (2.9%)	*0.861*
Hyperparathyroidism	6 (4.2%)	4 (5.3%)	2 (2.9%)	*0.528*
Gout	3 (2.1%)	2 (2.7%)	1 (1.5%)	*0.661*

3.2. Metabolic abnormalities

Serum laboratory values were comparable between the two groups. Among metabolic abnormalities, hypercalciuria was significantly more frequent in high-risk patients (44.0% vs. 23.5%, $p = 0.027$). The prevalence of hyperoxaluria, hyperparathyroidism, hypercalcemia, and proteinuria showed no significant differences. These findings suggest that conventional metabolic evaluation alone may not fully elucidate the increased stone risk observed in high-risk patients (Table 2).

Table 2
Laboratory features and the prevalence of metabolic abnormalities.

Serum values	Overall	High-risk	Low-risk	*p*
Calcium (mg/dL)	9.7 (9.1–10.0)	9.7 (9.18–10.0)	9.6 (9.0–10.0)	*0.311*
BUN (mg/dL)	14.4 (11.4–17.0)	14.2 (11.2–17.1)	15.0 (14.1–22.2)	*0.448*
Creatinine (mg/dL)	0.91 (0.78–1.07)	0.90 (0.76–1.06)	0.94 (0.67–1.35)	*0.069*
Uric acid (mg/dL)	6.0 (4.6–7.2)	6.0 (4.5–7.2)	5.95 (4.9–7.2)	*0.741*
eGFR (MDRD)	88.5 (77.8–90.0)	87.5 (77.8–90.0)	89.0 (35.5–90.0)	*0.282*
PTH (pg/mL)	40.2 (31.0–52.0)	40.5 (21.7–54.5)	39.4 (31.7–53.9)	*0.540*
Vitamin D (ng/mL)	21.6 (17.5–29.2)	20.6 (17.2–27.8)	22.1 (21.7–28.5)	*0.787*
Random urine				
pH	6.1 (5.5–6.7)	6.0 (5.5–6.8)	6.25 (5.3–6.8)	*0.848*
Calcium (mg/dL)	10.6 (6.9–20.3)	10.1 (6.6–20.6)	10.9 (6.7–17.2)	*0.780*
Creatinine (mg/dL)	120.4 (91.5–161.2)	118.0 (91.0–158.0)	130.2 (94.5–162.0)	*0.431*
Uric acid (mg/dL)	58.7 (40.5–73.8)	57.3 (39.0–74.5)	61.2 (43.1–78.7)	*0.905*
24-hour urine (mg/24 hours)				
Creatinine	1607 (1217–1858)	1541 (1214–1740)	1734 (1245–1946)	*0.236*
Sodium	174.5 (149.5–212.9)	171.5 (154.2–221.3)	176.5 (151.2–214.9)	*0.237*
Potassium	55.0 (47.0–75.7)	53.3 (45.8–73.6)	58.0 (50.1–78.3)	*0.214*
Na/K ratio	2.98 (2.51–3.95)	2.84 (2.50–3.98)	3.31 (2.74–3.99)	*0.652*
Calcium	229.0 (214.0–377.0)	239.0 (220.2–393.0)	215.0 (204.0–364.0)	*0.777*
Uric acid	726.0 (523.5–857.8)	702.5 (514.5–861.5)	756.0 (552–877.5)	*0.741*
Citrate	347.0 (263.0–645.0)	327.0 (234.0–644.5)	378.0 (292.0–660.5)	*0.992*
Oxalate	34.1 (29.5–48.1)	37.1 (30.2–48.5)	30.4 (27.8–45.1)	*0.413*
Phosphate	808.0 (634.0–1111)	866.0 (646.5–1128)	692.0 (612.0–985.5)	*0.502*

Serum values	Overall	High-risk	Low-risk	*p*
Protein	123.0 (84.7–278.3)	129.5 (88.6–280.0)	118.4 (80.3–248.0)	*0.580*
Albumin	15.0 (13.8–76.0)	16.5 (14.1–79.3)	14.1 (12.2–76.2)	*0.649*
Metabolic abnormalities				
Hypercalciuria	49 (34.3%)	33 (44.0%)	16 (23.5%)	*0.027*
Hyperoxaluria	11 (7.7%)	8 (10.7%)	3 (4.4%)	*0.191*
Hyperparathyroidism	6 (4.2%)	4 (5.3%)	2 (2.9%)	*0.528*
Hypercalcemia	10 (7.0%)	7 (9.3%)	3 (4.4%)	*0.290*
Proteinuria	35 (24.5%)	17 (22.7%)	18 (26.5%)	*0.533*

3.3. Stone composition

Calcium oxalate stones were the most common type, accounting for 78.7% of cases. Other stone types included uric acid stones (6.7%), struvite-containing mixed stones (5.3%), brushite (2.7%), cystine (1.3%), and calcium phosphate stones (1.3%) (Table 3). The distribution of stone components was consistent with previously reported epidemiologic data.

Table 3
Prevalence of stone composition in high-risk patients.

Calcium oxalate	**59 (78.7%)**
Calcium phosphate	1 (1.3%)
Mixed calcium	3 (4.0%)
Mixed primarily struvite	4 (5.3%)
Uric Acid	5 (6.7%)
Cystine	1 (1.3%)
Brushite	2 (2.7%)

3.4. Prevalence of monogenic gene mutations

Overall, gene mutations associated with urolithiasis were identified in 83 patients (58.1%). By risk group, high-risk patients demonstrated a significantly higher prevalence compared to low-risk patients (82.6% vs. 30.9%; $p < 0.001$). High-confidence monogenic gene mutations were detected in 57 (39.9%) in the overall group. Again, these mutations were significantly more common in the high-risk group (57.3% vs.

20.6%; $p < 0.001$). Risk-modifier genes were detected in 18.2% in the overall group, and were significantly more common in the high-risk group (25.3% vs. 10.3%; $p < 0.001$) (Table 4; Fig. 1.)

Table 4
Comparison of the prevalence of monogenic gene mutations in the overall cohort and according to risk groups.

Overall	**Overall**	**High-risk**	**Low-risk**	***p***
	83 (58.1%)	**62 (82.6%)**	**21 (30.9%)**	***< 0.001***
Level of evidence				*< 0.001*
High-confidence genes	57 (39.9%)	43 (57.3%)	14 (20.6%)	
Risk-modifier genes	26 (18.2%)	19 (25.3%)	7 (10.3%)	

3.5. Factors associated with high-confidence monogenic mutations

In univariate analysis, younger age and recurrent stone formation were associated with mutation positivity. After multivariate adjustment, recurrent stone formation remained the only independent factor associated with high-confidence monogenic mutations. Recurrent stone formers had approximately six-fold increased risk of harboring pathogenic mutations (OR 6.654, 95% CI 2.502–17.69; $p < 0.001$) (Table 5).

Table 5
Factors associated with positive high-confidence monogenic gene mutations.

	Univariate			Multivariate		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***
Age	1.045	1.029–1.067	*0.006*	1.082	0.802–1.461	*0.135*
Gender	2.066	0.882–4.837	*0.095*			
Body mass index	0.965	0.892–1.054	*0.388*			
Recurrence	4.091	1.687–9.918	*0.002*	6.654	2.502–17.69	*< 0.001*
Family history	0.341	0.092–1.258	*0.106*			
Calcium, serum	2.173	0.500–9.450	*0.301*			
BUN, serum	0.972	0.864–1.093	*0.631*			
Creatinine, serum	0.177	0.018–1.800	*0.141*			
Uric acid, serum	0.917	0.637–1.320	*0.642*			
eGFR	1.022	0.984–1.064	*0.251*			
Parathyroid hormone, serum	1.032	0.972–1.095	*0.300*			
Vitamin D, serum	0.964	0.890–1.045	*0.374*			
pH, random urine	0.632	0.242–1.650	*0.349*			
Calcium, random urine	0.948	0.846–1.063	*0.364*			
Creatinine, random urine	1.014	0.998–1.030	*0.090*			
Uric acid, random urine	1.043	0.994–1.093	*0.083*			

Supplementary Table 1. Distribution of monogenic genes associated with human urolithiasis in the overall cohort and according to risk groups.

	Univariate			Multivariate		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***
Creatinine, 24-hour urine	1.001	0.997–1.003	*0.934*			
Sodium, 24-hour urine	0.987	0.967–1.007	*0.187*			
Potassium, 24-hour urine	1.001	0.952–1.053	*0.967*			
Na/K ratio, 24-hour urine	0.467	0.142–1.540	*0.211*			
Calcium, 24-hour urine	0.997	0.990–1.003	*0.336*			
Uric acid, 24-hour urine	1.002	0.997–1.006	*0.505*			
Citrate, 24-hour urine	1.001	0.997–1.004	*0.850*			
Oxalate, 24-hour urine	0.975	0.931–1.022	*0.294*			
Phosphate, 24-hour urine	1.001	0.997–1.004	*0.749*			
Protein, 24-hour urine	0.999	0.996–1.002	*0.627*			
Albumin, 24-hour urine	0.998	0.993–1.003	*0.369*			
Hypercalciuria	0.263	0.030–2.347	*0.232*			
Hyperoxaluria	0.118	0.014–0.968	*0.047*			
Hyperparathyroidism	0.443	0.153–1.531	*0.456*			
Hypercalcemia	0.432	0.069–2.718	*0.371*			
Proteinuria	0.667	0.090–4.950	*0.691*			

Supplementary Table 1. Distribution of monogenic genes associated with human urolithiasis in the overall cohort and according to risk groups.

4. Discussion

In this prospective cross-sectional study, we investigated the prevalence and clinical significance of monogenic gene mutations associated with urolithiasis using a targeted next-generation sequencing panel comprising 47 genes related to renal stone formation. Several important findings were observed from our analysis. First, monogenic gene mutations were common in the overall cohort, with more than half of all patients harboring detectable variants associated with urolithiasis. Second, the prevalence of both overall mutations and high-confidence pathogenic variants was significantly higher in patients with high-risk clinical features compared with low-risk patients. Third, recurrent stone formation was identified as the strongest independent clinical predictor of pathogenic monogenic mutations. Together, these findings highlight the substantial genetic contribution to stone disease in selected patient populations and support the integration of genetic testing into the evaluation of patients with high-risk urolithiasis.

The growing recognition of genetic contributions to urolithiasis has been driven by advances in genomic sequencing technologies. Historically, urolithiasis was considered primarily an environmentally-driven disorder influenced by dietary factors, metabolic abnormalities, and lifestyle variables [5]. However, increasing evidence demonstrates that hereditary disorders affecting renal tubular transport, mineral metabolism, and metabolic pathways play a substantial role in stone formation [1]. Recent studies estimate that monogenic causes account for approximately 15–30% of urolithiasis cases in selected populations, particularly among pediatric patients and those with early-onset disease.

Our findings are consistent with this expanding body of literature; however, unlike previous studies that focused exclusively on pediatric cohorts or rare hereditary disorders, our study evaluated a clinically heterogeneous group of patients undergoing evaluation for urolithiasis. Despite this broader population, we observed a remarkably high prevalence of genetic mutations, particularly among high-risk individuals. More than 80% of patients in the high-risk group carried at least one genetic variant associated with urolithiasis, and more than half had high-confidence pathogenic mutations. These findings emphasize the importance of appropriate patient selection when considering genetic testing for patients with urolithiasis.

Among the risk factors evaluated in this study, recurrent stone formation was identified as the strongest predictor of pathogenic monogenic mutations. Multivariate logistic regression demonstrated that recurrent stone formers had more than six-fold higher odds of harboring high-confidence pathogenic variants. This observation is biologically plausible, as many monogenic disorders affecting renal tubular transport lead to persistent metabolic abnormalities that predispose patients to repeated stone formation [17].

Previous studies have similarly highlighted recurrence as a key indicator of genetic stone disease [18]. Disorders such as primary hyperoxaluria, cystinuria, distal renal tubular acidosis, and hereditary phosphate-handling disorders often present with recurrent stones beginning at a relatively young age [19]. Failure to recognize these conditions early may lead to repeated surgical interventions, progressive renal damage, and unnecessary healthcare costs. For example, a 34-year-old male patient in our cohort

underwent multiple surgical interventions for recurrent calcium oxalate monohydrate stones, with early recurrence after each procedure. Metabolic evaluation suggested primary hyperoxaluria, and NGS identified a *GRHPR* mutation, confirming primary hyperoxaluria type 2 [20, 21]. Without NGS, accurate subtype classification would have been challenging, and the appropriateness of initiating pyridoxine therapy, beyond standard treatment with potassium citrate, would have remained uncertain. Overall, identifying genetic causes in recurrent stone formers has important clinical implications for long-term management.

Interestingly, conventional metabolic abnormalities were largely comparable between the high- and low-risk groups in our study, with the exception of hypercalciuria, which was more prevalent among high-risk patients. This finding suggests that routine metabolic evaluation alone may not fully capture the underlying pathophysiologic mechanisms driving stone formation in genetically predisposed patients. In many hereditary stone disorders, metabolic disturbances may fluctuate over time or remain within borderline ranges, making them difficult to detect using standard laboratory testing [22, 23]. Genetic testing may therefore provide additional diagnostic information that complements traditional metabolic evaluation. Identifying the underlying molecular defect can clarify the pathogenesis of stone formation and guide targeted management strategies.

Another important finding in our study was the wide spectrum of genes identified in association with urolithiasis. The targeted gene panel used in this study included both well-established monogenic stone genes and susceptibility genes associated with altered mineral metabolism or tubular function. This approach reflects the evolving understanding that kidney stone disease exists along a genetic continuum ranging from highly penetrant Mendelian disorders to polygenic susceptibility influenced by environmental factors.

High-confidence monogenic stone genes identified in our cohort included genes associated with oxalate metabolism, cystine transport, renal tubular acidosis, phosphate transport disorders, and calcium metabolism. Although the majority of genes identified were high-confidence genes, we also identified variants in several risk-modifier genes. These genes may not independently cause stone disease but may increase susceptibility through subtle alterations in mineral handling or tubular transport [1, 13, 14]. The clinical significance of such variants remains an area of active investigation. Future studies integrating genomic, metabolomic, and environmental data may help clarify how these genetic factors interact to influence stone formation.

One concern regarding the routine use of genetic testing in urolithiasis is its cost-effectiveness. Historically, genomic testing has been limited by high costs and limited accessibility. However, advances in NGS technology have dramatically reduced the cost of genetic analysis, making targeted gene panels increasingly feasible in clinical practice. Our results suggest that patients with specific features, including recurrent disease, early disease onset, or family history, represent a subgroup in whom genetic testing may confer diagnostic value. Ultimately, genetic testing may reduce healthcare costs by enabling earlier diagnosis and more effective disease prevention. Indeed, urolithiasis is associated with

substantial healthcare expenditures due to repeated imaging studies, emergency department visits, surgical interventions, and hospitalizations. By identifying genetic etiologies early in the disease course, targeted preventive strategies can be implemented to reduce future costs. For example, disorders such as primary hyperoxaluria, cystinuria, and Dent disease have well-established molecular causes that can be confirmed through genetic testing and managed accordingly [24, 25].

Our study has several limitations that should be considered when interpreting the results. First, the study was conducted at a single tertiary referral center, which may pose referral bias toward more complex or recurrent cases. As a result, the prevalence of genetic mutations observed in this cohort may be higher than that seen in the general population. Second, although the targeted NGS panel included a comprehensive set of 47 genes associated with nephrolithiasis, it may not capture all potential genetic contributors to stone disease. Whole-exome or whole-genome sequencing may identify additional variants not included in our panel. Third, the cross-sectional design of this study limits the ability to assess long-term clinical outcomes associated with specific genetic mutations.

Future research should focus on multicenter studies involving larger and more diverse patient populations to validate these findings. Longitudinal studies examining genotype-phenotype correlations will also be essential to determine how specific genetic mutations influence stone recurrence, renal function decline, and treatment response. In addition, integration of genomic data with detailed metabolic profiling may further improve our understanding of the complex pathophysiology underlying kidney stone disease.

Despite these limitations, our study provides important evidence supporting the clinical relevance of genetic testing in patients with urolithiasis. By identifying a strong association between high-risk clinical features and pathogenic gene mutations, our findings offer a practical framework for selecting patients who are most likely to benefit from genetic evaluation.

5. Conclusions

This study demonstrates that monogenic gene mutations associated with urolithiasis are highly prevalent, particularly in patients with high-risk clinical features such as recurrent stone formation and early disease onset. High-confidence pathogenic mutations were significantly detected in the high-risk group, and recurrent stone disease emerged as the strongest independent predictor of genetic etiology. These findings highlight the role of genetic factors in the pathogenesis of nephrolithiasis and support the implementation of targeted genetic testing strategies that may provide personalized preventive interventions in selected patients.

Declarations

6. Data Availability Statement

Data supporting this study's findings are available from the corresponding author upon reasonable request. The original dataset is not publicly available due to the institutional review board policy.

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9. CRediT authorsip contribution statement

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Figures

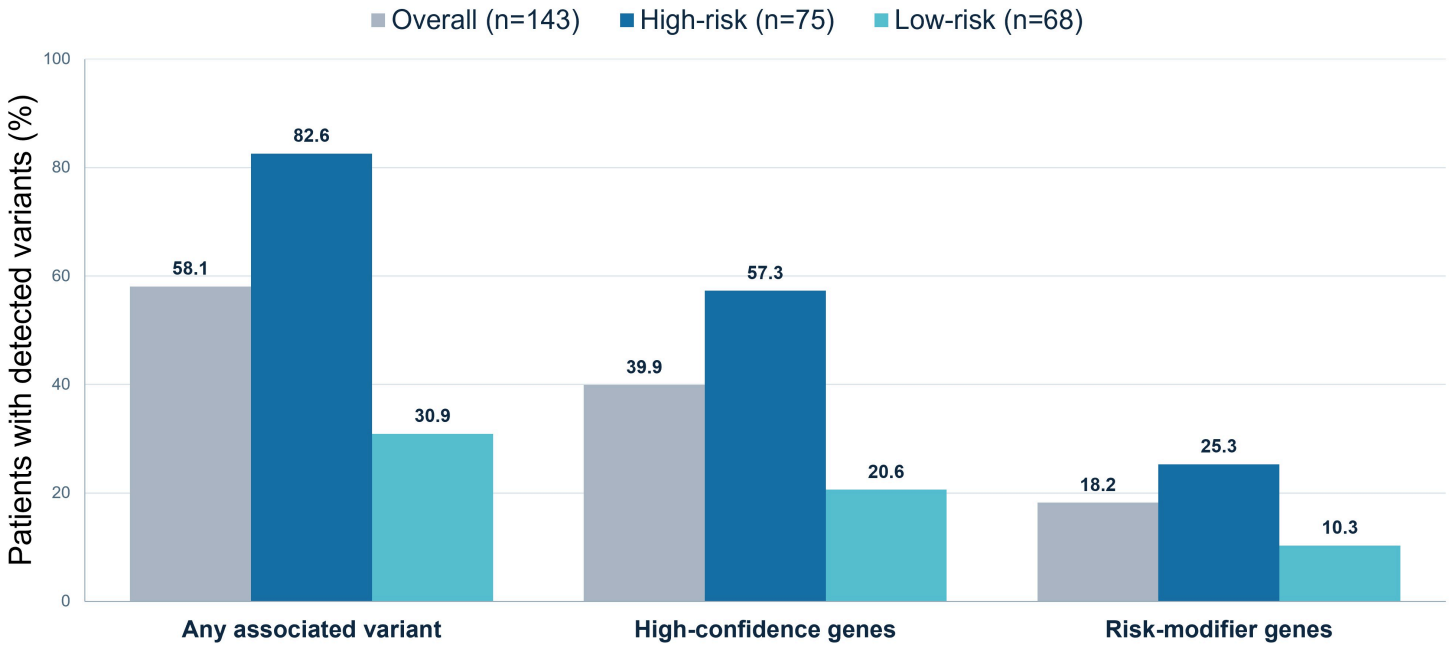


Figure 1

Legend not included with this version.

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