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ORIGINAL RESEARCH

Assessment of Metabolic, Clinical and Radiological Risk Factors for Nephrolithiasis in Autosomal Dominant Polycystic Kidney Disease: A Single-Center Retrospective Study

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ABSTRACT

Autosomal dominant polycystic kidney disease (ADPKD) is a common monogenic disorder associated with an increased risk of nephrolithiasis. This study aimed to evaluate the clinical, metabolic, and radiological risk factors contributing to kidney stone formation in patients with ADPKD. A total of 55 patients followed in the nephrology outpatient setting at Bursa City Hospital between January 2022 and January 2025, with available non-contrast abdominopelvic CT scans, were retrospectively analyzed. Demographic data, laboratory values, radiological characteristics, and 24-hour urine analyses were recorded. Kidney stones were detected in 58.2% of patients based on CT reports. Macroscopic hematuria was observed exclusively in the stone-positive group. In multivariate logistic regression analysis, the presence of hepatic cysts (OR: 4.34) and increased 24-hour urinary calcium excretion (OR: 1.01) were identified as independent risk factors for nephrolithiasis. No significant association was found between stone formation and urinary citrate or oxalate levels. The number of patients receiving Tolvaptan therapy was equal between the two groups, limiting the assessment of its potential effect on stone formation. Although the prevalence of hypertension was higher in the stone-positive group, the difference was not statistically significant. The higher prevalence of nephrolithiasis observed in our cohort compared to the literature suggests that even asymptomatic ADPKD patients may benefit from non-contrast CT screening. Evaluating parameters such as hypercalciuria and hepatic cysts may aid in the development of individualized monitoring and management strategies.

Keywords: Autosomal dominant polycystic kidney disease. Nephrolithiasis. Risk factors. Radiological assessment.

Otozomal Dominant Polikistik Böbrek Hastalığında Nefrolitiazis İçin Metabolik, Klinik ve Radyolojik Risk Faktörlerinin Değerlendirilmesi: Tek Merkezli Retrospektif Bir Çalışma

ÖZET

Otozomal dominant polikistik böbrek hastalığı (ODPKBH), böbrek taşı gelişimi açısından artmış risk barındıran bir monogenik hastalıktır. Bu çalışmada, ODPKBH tanılı bireylerde böbrek taşı oluşumuna katkıda bulunabilecek klinik, metabolik ve radyolojik risk faktörlerinin değerlendirilmesi amaçlanmıştır. Ocak 2022 - Ocak 2025 tarihleri arasında Bursa Şehir Hastanesi Ayaktan Nefroloji Polikliniği'nde takip edilen ve non-kontrast batın BT görüntülemesi mevcut olan, 55 ODPKBH hastasının verileri retrospektif olarak incelendi. Demografik, laboratuvar ve radyolojik özellikler ile 24 saatlik idrar analizleri kaydedildi. Hastaların %58,2'sinde BT raporlarında taş varlığı tespit edildi. Makroskopik hematüri sadece taş saptanan grupta gözlendi. Çok değişkenli lojistik regresyon analizinde, karaciğer kisti varlığı (OR: 4,34) ve 24 saatlik idrarda artmış kalsiyum atılımı (OR: 1,01) bağımsız risk faktörleri olarak belirlendi. Sitrat ve oksalat düzeyleri ile taş varlığı arasında anlamlı ilişki saptanmadı. Tolvaptan tedavisi alan hasta sayısı eşit olduğundan bu ilacın taş üzerine etkisi değerlendirilemedi. Taş saptanan grupta hipertansiyon oranı yüksek olmakla birlikte istatistiksel anlamlılık izlenmedi. Çalışmamızda literatüre kıyasla daha yüksek taş prevalansı tespit edilmesi, asemptomatik ODPKBH hastalarında dahi non-kontrast BT ile taş taramasının değerli olabileceğini düşündürmektedir. Hiperkalsiüri ve karaciğer kisti varlığı gibi parametrelerin değerlendirilmesi, kişiye özgü takip ve tedavi planlarının oluşturulmasına katkı sağlayabilir.

Anahtar Kelimeler: Otozomal dominant polikistik böbrek hastalığı. Nefrolitiyazis. Risk faktörleri. Radyolojik değerlendirme.

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Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disorder characterized by bilateral renal cysts and affects approximately 1 in 400 to 1,000 individuals, making it one of the most common monogenic kidney diseases[1]. The diagnosis is typically made in adulthood, and approximately 50% of patients progress to end-stage renal disease (ESRD) around the age of 60[2]. The disease is not

limited to the kidneys; it also affects multiple organ systems such as the liver, pancreas, cerebral vasculature, and cardiac valves. The most common extrarenal manifestation is hepatic cysts[3]. Nephrolithiasis is one of the important complications in the course of ADPKD. The prevalence of kidney stone formation in ADPKD patients is higher than in the general population and has been reported to range from 20% to 36%[4–5]. The increased risk of stone formation is associated with anatomical distortion due to cystic structures, urinary stasis, recurrent infections, and metabolic abnormalities such as hypercalciuria, hypocitraturia, and hyperuricosuria[6–7]. Kidney stones in this patient group may be linked to recurrent pain, hematuria, infections, and a more rapid decline in renal function[8–9]. However, the clinical, metabolic, and radiological risk factors contributing to stone formation in ADPKD patients have not yet been fully clarified. This study aims to evaluate retrospectively the potential risk factors for nephrolithiasis in patients diagnosed with ADPKD and to determine the differences between individuals with and without kidney stones.

Material and Method

This retrospective study was conducted in the Nephrology Department of Bursa City Hospital and aimed to evaluate clinical and metabolic factors associated with kidney stone formation in patients diagnosed with autosomal dominant polycystic kidney disease (ADPKD) between January 2022 and January 2025. The study was approved by the local ethics committee with decision number 2025-3/7, dated February 5, 2025. A total of 55 patients aged 18 years and older, with a confirmed diagnosis of ADPKD based on imaging (ultrasonography, CT, or MRI) and/or family history, and who had available non-contrast abdominopelvic CT scans, were included in the study. The presence of kidney stones was determined based on CT reports that included the statement “millimetric stones are present” and/or provided the stone size in millimeters. Patients were classified as either “stone present” or “stone absent” accordingly. Hepatic cysts were considered present only if explicitly reported in radiology reports. Renal volumes were calculated by multiplying sagittal length, width, and depth measurements by the ellipsoid formula constant (0.523). These volume values were then evaluated according to the Mayo Clinic classification system, taking into account the patient’s age and height. Demographic (age, sex, body mass index, smoking history), clinical (hypertension, comorbidities, use of antihypertensive drugs, Tolvaptan use, and family history), and laboratory data were obtained from the hospital’s electronic medical records. Laboratory parameters included complete blood count, serum creatinine, eGFR, uric acid, albumin, fasting blood glucose, parathyroid hormone (PTH), AST, ALT, lipid profile, urine specific gravity, and pH. Proteinuria was evaluated using either spot urine samples or 24-hour urine collections. Additionally, 24-hour urinary parameters including volume, calcium, phosphorus, uric acid, oxalate, potassium, and citrate levels were analyzed.

Statistical analysis

The normality of continuous variables was assessed using the Shapiro-Wilk test. According to the results of the normality test, variables that conform to normal distribution were expressed as mean ± standard deviation and variables that do not conform to normal distribution were expressed as median (minimum: maximum) values; categorical variables were expressed as n (%). In the comparisons between two groups, Independent Samples t test was used in case of conformity to normal distribution and Mann Whitney U test was used in case of non-conformity to normal distribution. Categorical variables were compared between groups using Pearson Chi-Square test, Fisher's Exact Chi-Square test and Fisher Freeman Halton test. Logistic regression analysis was used to determine the risk factors thought to be effective on the development of kidney stones. For statistical analyses, SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) programme was used and type I error rate was accepted as 5%.

Results

A total of 55 patients with ADPKD were included in the study, of whom 32 (58.2%) had kidney stones and 23 (41.8%) did not. In terms of demographic and clinical characteristics, there were no statistically significant differences between the stone-positive and stone-negative groups in age, sex, body mass index (BMI), smoking status, family history, or hypertension ($p>0.05$; Table I). No significant differences were observed between the groups regarding the use of antihypertensive medications including RAS blockers, calcium channel blockers, beta-blockers, diuretics, alpha-blockers, or Tolvaptan therapy ($p>0.05$; Tables II and IV). Although hepatic cysts were more frequently observed in the stone-positive group, the difference did not reach statistical significance ($p=0.134$; Table II). Macroscopic hematuria was present in 22.6% of the stone-positive patients, while none of the stone-negative patients had this finding. This difference was statistically significant ($p=0.033$; Table II). Regarding laboratory parameters, no significant differences were found between the groups in hemoglobin, serum creatinine, eGFR, uric acid, parathyroid hormone, fasting glucose, lipid profile, electrolytes, albumin, or proteinuria ($p>0.05$; Table III). In the 24-hour urine analysis, parameters including urine volume, citrate, oxalate, calcium,

phosphorus, uric acid, potassium, urine density, and pH showed no significant differences between the groups (p>0.05; Table IV). Similarly, total renal volume and Mayo Clinic imaging classification stages did not differ significantly between groups (Table IV). Logistic regression analysis revealed that, in the multivariate model, the presence of hepatic cysts was identified as an independent risk factor for kidney stone formation (OR: 4.34; 95% CI: 1.05–17.93; p=0.042). In addition, each 1 mg/day increase in 24-hour urinary calcium excretion was associated with a 1.01-fold increased risk of nephrolithiasis (OR: 1.01; 95% CI: 1.00–1.02; p=0.041; Table V). The final multivariate logistic regression model was found to be statistically significant (model p=0.022), with acceptable goodness of fit (Hosmer-Lemeshow test, p=0.244).

Table I. Comparison of demographic and clinical characteristics between patients with and without kidney stones

Variable	Total (n=55)	Stone Present (n=32)	Stone Absent (n=23)	p-value
Age (years)	45.5±12.5	47.4±9.9	42.8±15.3	0.216[a]
Sex				
• Male	28 (50.9%)	18 (56.3%)	10 (43.5%)	0.350[b]
• Female	27 (49.1%)	14 (43.8%)	13 (56.5%)	
BMI (kg/m²)	26.8±3.4	27.4±3.1	26.1±3.7	0.156[a]
Smoking				
• Yes	20 (36.4%)	11 (34.4%)	9 (39.1%)	0.718[b]
• No	35 (63.6%)	21 (65.6%)	14 (60.9%)	
Family history				
• Yes	45 (81.8%)	25 (78.1%)	20 (87%)	0.494[c]
• No	10 (18.2%)	7 (21.9%)	3 (13%)	
Hypertension				
• Yes	33 (60%)	22 (68.8%)	11 (47.8%)	0.118[b]
• No	22 (40%)	10 (31.3%)	12 (52.2%)	

Data are expressed as mean ± standard deviation, median (minimum: maximum) and n%.
a: Independent Sample t test, b: Pearson Chi-Square test, c: Fisher's Exact Chi-Square test
BMI: Body Mass Index

Table II. Comparison of antihypertensive medication use, urinary complications, and radiological findings (Liver Cyst) between patients with and without kidney stones

	Total (n=55)	Stone Present (n=32)	Stone Absent (n=23)	p-value
Renin–Angiotensin System Blocker (RAS Blocker)				
• Yes	30 (54.5%)	19 (59.4%)	11 (47.8%)	0.396[b]
• No	25 (45.5%)	13 (40.6%)	12 (52.2%)	
Calcium Channel Blocker (CCB)				
• Yes	9 (16.4%)	8 (25.0%)	1 (4.3%)	0.064[c]
• No	46 (83.6%)	24 (75.0%)	22 (95.7%)	
Beta Blocker				
• Yes	8 (14.8%)	5 (16.1%)	3 (13.0%)	>0.99[c]
• No	46 (85.2%)	26 (83.9%)	20 (87.0%)	
Diuretic				
• Yes	13 (23.6%)	8 (25.0%)	5 (21.7%)	0.779[b]
• No	42 (76.4%)	24 (75.0%)	18 (78.3%)	
Alpha Blocker				
• Yes	8 (14.5%)	5 (15.6%)	3 (13.0%)	>0.99[c]
• No	47 (85.5%)	27 (84.4%)	20 (87.0%)	
Urinary Tract Infection (UTI)				
• Yes	2 (3.8%)	0 (0.0%)	2 (9.5%)	0.158[c]
• No	50 (96.2%)	31 (100.0%)	19 (90.5%)	
Macroscopic Hematuria				
• Yes	7 (13.5%)	7 (22.6%)	0 (0.0%)	0.033[c]
• No	45 (86.5%)	24 (77.4%)	21 (100.0%)	
Hepatic Cyst				
• Yes	35 (63.6%)	23 (71.9%)	12 (52.2%)	0.134[b]
• No	20 (36.4%)	9 (28.1%)	11 (47.8%)	

Data are expressed as n(%)
b: Pearson Chi-Square test, c: Fisher's Exact Chi-Square test

Table III. Comparison of biochemical and hematological parameters between patients with and without kidney stones

Parameter	Total (n=55)	Stone Present (n=32)	Stone Absent (n=23)	p-value
Hemoglobin (g/dL)	13.6±1.8	13.5±1.8	13.5±2.1	0.926[a]
Creatinine (mg/dL)	1 (0.6-6.1)	1 (0.6-6.1)	0.9 (0.6-4.4)	0.298[d]
eGFR (mL/min)	72.4±32.1	67.5±30.3	77.1±36.7	0.293[a]
Uric Acid (mg/dL)	5.1 (2.5-9.5)	5.9 (2.5-8.5)	5.1 (3-38)	0.544[d]
Parathyroid Hormone (pg/mL)	51.1 (13.5-287)	51.2 (20.4-287)	52.1 (13.5-243)	0.850[d]
Fasting Glucose (mg/dL)	93.5 (71-201)	94.5 (71-141)	89.5 (76-201)	0.679[d]
Total Cholesterol (mg/dL)	191.5±36.2	208.7±34.1	189±37.8	0.055[a]
LDL (mg/dL)	125.5±31	131.3±28.4	115.3±32.5	0.064[a]
Triglycerides (mg/dL)	123 (51-330)	119.5 (51-330)	120.5 (54-270)	0.912[d]
HDL (mg/dL)	48.4±12.9	49.9±13.5	46.3±12.1	0.334[a]
Sodium (mmol/L)	140.7±2.3	141.2±2.3	140.2±2.1	0.092[a]
Potassium (mmol/L)	4.4 (3-6.7)	4.4 (3-6.7)	4.3 (3.8-5.2)	0.114[d]
Calcium (mg/dL)	9.3 (8.4-10.5)	9.3 (7.1-10.5)	9.3 (8.4-10.1)	0.712[d]
Phosphorus (mg/dL)	3.3 (2.5-5.1)	3.2 (2.4-5.1)	3.6 (2-4.9)	0.206[d]
Albumin (g/L)	44.7±2.6	44.9±2.4	44.5±2.9	0.522[a]
Proteinuria (mg/day)	130 (30-4152)	128.2 (30-4152)	130 (30-3134)	0.791[d]

Data are expressed as mean ± standard deviation and median (minimum: maximum)
a: Independent Sample t test, d: Mann-Whitney U test

Table IV. Comparison of radiological and 24-hour urinary parameters between patients with and without kidney stones

Parameter	Total (n=55)	Stone Present (n=32)	Stone Absent (n=23)	p-value
Total Kidney Volume (mL)	1412 (273–6902)	1344 (399–5698)	1412 (273–6902)	0.682[d]
Mayo Stage				0.688[e]
• 1A	1 (1.8%)	0	1 (4.3%)	
• 1B	17 (30.9%)	10 (31.3%)	7 (30.4%)	
• 1C	14 (25.5%)	8 (25%)	6 (26.1%)	
• 1D	18 (32.7%)	12 (37.5%)	6 (26.1%)	
• 1E	5 (9.1%)	2 (6.3%)	3 (13%)	
Urine Volume (mL/day)	2300 (900–8900)	2600 (800–6000)	2500 (1300–8900)	0.925[d]
Urine Specific Gravity	1014.8 ± 7.4	1011.9 ± 6	1015.4 ± 7.6	0.073[a]
Urine pH	5.5 (5–6.5)	5.5 (5–6.5)	5.5 (5–7)	0.754[d]
24h Urinary Citrate (mg/day)	309 (15–1615)	240 (13.5–1615)	249 (6–708)	0.709[d]
24h Urinary Oxalate (mg/day)	22.4 (4.2–168.6)	18.7 (3.5–66.3)	16.5 (0.8–168.6)	0.853[d]
24h Urinary Uric Acid (mg/day)	403.2 (181.8–1097)	355 (100.5–1097)	420 (147.2–873.6)	0.428[d]
24h Urinary Calcium (mg/day)	102.7 (29.2–321.5)	95.7 (8.8–321.5)	108.9 (19.6–245.3)	0.900[d]
24h Urinary Phosphorus (mg/day)	690.8 (228–1650.5)	567.6 (87.1–1650.5)	624.9 (266.2–1528.8)	0.759[d]
24h Urinary Potassium (mmol/day)	56.6 (17.6–111.4)	53.5 (8.3–111.4)	47.9 (26.7–140.6)	0.479[d]
Tolvaptan				0.707[c]
• Receiving	8 (14.5%)	4 (12.5%)	4 (17.4%)	
• Not Receiving	47 (85.5%)	28 (87.5%)	19 (82.6%)	

Data are expressed as mean ± standard deviation and median (minimum: maximum)
a: Independent Sample t test, c: Fisher's Exact Chi-Square test, d: Mann-Whitney U test,
e: Fisher-Freeman-Halton test

Table V. Univariate and multivariate logistic regression analysis of risk factors for kidney stone formation

	OR (95% CI)	p	OR (95% CI)	p
Age	1.03 (0.99–1.08)	0.184		
Sex (Male)	0.59 (0.20–1.76)	0.351		
BMI	1.13 (0.95–1.34)	0.157		
Family history	0.54 (0.12–2.34)	0.407		
Hypertension history	2.4 (0.79–7.27)	0.122		
Smoking	0.82 (0.27–2.47)	0.718		
UTI	-	0.999		
Macroscopic hematuria	-	0.999		
Hepatic cyst (Present)	2.34 (0.76–7.21)	0.138	4.34 (1.05–17.93)	0.042
Hb	1.01 (0.77–1.34)	0.924		
Creatinine	1.23 (0.71–2.13)	0.467		
GFR (ml/min)	0.99 (0.98–1.01)	0.288		
Uric acid	0.95 (0.82–1.09)	0.446		
PTH	0.99 (0.99–1.01)	0.872		
Fasting glucose	0.99 (0.96–1.01)	0.336		
Total cholesterol	1.02 (0.99–1.03)	0.062		
LDL	1.02 (0.99–1.04)	0.072		
TG	1.00 (0.99–1.01)	0.978		
HDL	1.02 (0.98–1.07)	0.329		
Sodium	1.25 (0.96–1.62)	0.097		
Potassium	2.06 (0.59–7.19)	0.258		
Calcium	1.11 (0.38–3.18)	0.853		
Phosphorus	0.59 (0.25–1.39)	0.227		
Albumin	1.07 (0.87–1.32)	0.515		
Proteinuria (mg/day)	1.00 (0.99–1.00)	0.750		
Total Kidney Volume	1.00 (1.00–1.00)	0.800		
Urine Volume	1.00 (1.00–1.00)	0.456		
Urine Density	0.93 (0.85–1.01)	0.078		
Urine pH	0.80 (0.28–2.28)	0.676		
24h Urine Citrate (mg/day)	1.00 (0.99–1.00)	0.918		
24h Urine Oxalate (mg/day)	0.99 (0.97–1.02)	0.526	0.98 (0.95–1.01)	0.122
24h Urine Uric Acid (mg/day)	0.99 (0.99–1.00)	0.512		
24h Urine Calcium (mg/day)	1.00 (0.99–1.02)	0.625	1.01 (1.00–1.02)	0.041
24h Urine Phosphorus (mg/day)	1.00 (0.99–1.00)	0.580		
24h Urine Potassium (mmol/day)	1.01 (0.98–1.03)	0.582		
Tolvaptan	0.68 (0.15–3.05)	0.613		

OR: Odds Ratio, CI: Confidence Interval
For the variables, the following reference categories were used: "Female" for sex, "Absent" for family history, "Absent" for history of hypertension, "Non-smoker" for smoking status, "Absent" for urinary tract infection (UTI), "Absent" for macroscopic hematuria, "Absent" for liver cyst, and "Not receiving" for tolvaptan use.

Discussion and Conclusion

In this study, the prevalence of kidney stones was found to be higher (58.2%) compared to the rates reported in the literature for patients with ADPKD (20–36%). This difference may be attributed to several factors. Given the high sensitivity of CT in detecting stones—especially small or asymptomatic ones—this imaging modality may have contributed to the higher observed prevalence. Furthermore, in this study, stone presence was not limited to large or clinically significant calculi; phrases such as "millimetric stones are present" in CT reports were also included in the assessment. This broader approach may have resulted in a higher reported prevalence by encompassing a wider spectrum of stone burden.

In the current study, macroscopic hematuria was observed only in patients with kidney stones (22.6%) and was not detected in the stone-free group. This finding suggests that nephrolithiasis may be one of the causes of hematuria in patients with ADPKD. In ADPKD, hematuria typically arises from cyst rupture, infection, papillary necrosis, or nephrolithiasis. The association between stone disease and hematuria has been reported in the literature. As noted by Torres et al. in *UpToDate*, kidney stones are considered one of the common causes of hematuria in ADPKD patients[9]. Therefore, when hematuria is present in these patients, nephrolithiasis should be evaluated in addition to cyst-related causes.

In the present study, the presence of liver cysts was identified as an independent risk factor for kidney stone formation in ADPKD patients. This relationship may be explained by the distortion of anatomical structures and the subsequent urinary stasis caused by the extensive cyst burden. Although data on this topic are limited in the literature, the study by Onur Kaygısız et al. also reported a significantly higher prevalence of kidney stones in patients with liver cysts [10]. These findings support the results of our study and suggest that liver cysts, although typically considered benign extrarenal manifestations, may contribute to nephrolithiasis through anatomical or physiological changes.

Twenty-four-hour urinary calcium excretion was found to be a statistically significant independent risk factor for stone formation in multivariate logistic regression analysis. This finding supports the established role of hypercalciuria in the pathogenesis of calcium oxalate stones. Similarly, numerous studies have reported that hypercalciuria increases urinary supersaturation, thereby promoting crystallization and facilitating stone formation[11,12]. Furthermore, studies by Worcester and Coe emphasized that hypercalciuria is a key predisposing factor in both sporadic and familial stone disease[13]. Although the use of diuretics did not differ significantly between the stone-positive and stone-negative groups in our study, the specific types of diuretics were not analyzed separately. This may be relevant, as thiazide diuretics are known to reduce urinary calcium excretion and potentially lower the risk of calcium-based stones, whereas loop diuretics may increase calciuria and promote stone formation. The absence of detailed diuretic subclass data constitutes a minor limitation in evaluating their potential impact on nephrolithiasis risk.

However, in the current study, no statistically significant association was found between 24-hour urinary citrate or oxalate levels and the presence of stones. In contrast, the literature highlights hypocitraturia (low 24-hour urinary citrate) and hyperoxaluria (elevated oxalate excretion) as major metabolic abnormalities predisposing to stone formation[14,15]. Citrate inhibits crystallization by forming soluble complexes with urinary calcium, while oxalate is a major contributor to calcium oxalate stone formation. Although some studies have reported more frequent hypocitraturia in patients with stones, this difference has not always reached statistical significance[6,16].

Another known stone inhibitor is magnesium, which impedes calcium oxalate crystallization by competing with calcium to form soluble oxalate complexes. Several studies have identified low 24-hour urinary magnesium levels as a significant risk factor for calcium oxalate stones[17,18]. In the current study, 24-hour urinary magnesium was not measured due to laboratory requirements for acidified collection containers, which constitutes one of the limitations of this study.

In the current cohort, the mean total kidney volumes of patients with and without stones were similar (1344 mL vs. 1412 mL), and most patients in both groups were classified as Mayo Clinic imaging classes 1B and 1D. Similarly, a cross-sectional study conducted in Türkiye also reported no significant difference in total kidney volume between ADPKD patients with and without stones[19]. Conversely, the study by Grampsas et al. found that patients with stone disease had a greater number of renal cysts and larger dominant cysts[6]. Likewise, in another study by Nishiura et al., ADPKD patients with stones had significantly larger total kidney volumes[16]. These findings suggest that, in addition to total kidney volume, the distribution of cyst burden and the size of dominant cysts may play a role in stone pathophysiology.

Another limitation of the current study was the small number of patients receiving tolvaptan therapy, which precluded a comparative analysis with untreated patients. Tolvaptan, a vasopressin V2 receptor antagonist, is the first and only approved pharmacological treatment to slow disease progression

in autosomal dominant polycystic kidney disease (ADPKD). It reduces cyst expansion and kidney growth by increasing urine output through decreased water reabsorption in the renal tubules[20]. Theoretically, increased urine volume may reduce urinary supersaturation and thereby lower the risk of nephrolithiasis. However, clinical evidence regarding the preventive effect of tolvaptan on stone formation remains limited. In our study, the number of patients treated with tolvaptan was equal in both groups (4 vs. 4).

Hypertension is another factor worth considering in the pathogenesis of nephrolithiasis in ADPKD. In our study, the prevalence of hypertension was higher among patients with stones compared to those without (68.8% vs. 48.8%), although this difference did not reach statistical significance. Some studies have explored the association between hypertension and nephrolithiasis. For instance, Borghi et al. reported a significantly increased risk of stone formation in individuals with hypertension, especially when accompanied by obesity, which may be related to increased oxaluria, calciuria, and urinary supersaturation of calcium oxalate and uric acid [21]. Madore et al. similarly found a higher prevalence of hypertension in individuals with a history of nephrolithiasis[22]. However, both studies were conducted in the general population, not specifically among ADPKD patients.

Other limitations of this study include its single-center design and relatively small sample size, which may limit the generalizability of our findings and reduce statistical power in subgroup analyses. Nevertheless, our study also possesses notable strengths. The comprehensive evaluation of clinical, laboratory, and radiological data; the inclusion of 24-hour urine analyses in a substantial portion of patients; and the use of the updated Mayo Clinic imaging classification system to assess kidney volumes enhance the methodological rigor of this research. Furthermore, the investigation of extrarenal findings such as liver cysts in relation to nephrolithiasis represents a relatively novel approach in the literature.

In conclusion, this study provides a multidimensional analysis of clinical, metabolic, and radiological risk factors contributing to nephrolithiasis in ADPKD patients. It emphasizes that hypercalciuria and the presence of liver cysts may be particularly important parameters warranting close attention. The higher prevalence of kidney stones observed in our cohort compared to the literature suggests that non-contrast abdominal CT may be a valuable tool for detecting stones, even in asymptomatic patients. These findings underscore the importance of early recognition of stone risk in ADPKD and support the need for individualized patient management strategies.

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