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Effect of Potassium Citrate Therapy on Biochemical Parameters and Stone Burden in Patients with Recurrent Kidney Stones: A Prospective Comparative Study

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Abstract

Background: This study aimed to evaluate biochemical risk factors in patients with recurrent kidney stones and to assess the pharmacological role of citrate-based therapy compared with standardised dietary modification and increased water intake alone.

Methods: An 80 adult patients with recurrent kidney stones were allocated into two groups. Group 1 included 40 patients who received standardized dietary modification and increased water intake only, whereas Group 2 included 40 patients who received potassium citrate effervescent tablets (20 mEq) twice daily for one month, in addition to the same standardized dietary modification and increased water intake. The assessments included blood biochemical parameters and ultrasonographic evaluation of stone number and size. Stones obtained through spontaneous passage during the study period were physically characterized and chemically analyzed using a qualitative/semi-quantitative chemical method to determine their composition.

Results: Stone number decreased significantly (p=0.030) in Group 2 (0.60±0.71) compared to Group 1 (1.90±3.60). Stone analysis showed that calcium oxalate stones were the predominant type in both groups, followed by uric acid-containing stones. Complete stone resolution was observed in 35% of patients in Group 2 compared with 0% in Group 1, while new stone formation was less frequent in Group 2.

Conclusion: Biochemical and radiological outcomes favoured potassium citrate therapy. Potassium citrate showed promising short-term improvements, but larger randomized studies with longer follow-up are needed.

تأثير العلاج بسترات البوتاسيوم في المؤشرات الكيميائية الحيوية وعبء الحصوات لدى مرضى تحصّي الكلى المتكرر: دراسة مقارنة مستقبلية

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الخلاصة:

هدفت هذه الدراسة إلى تقييم العوامل البيوكيميائية لدى المرضى الذين يعانون من حصوات الكلى المتكررة ولتقييم الدور الدوائي للعلاج القائم على السترات مقارنةً بالتعديلات الغذائية القياسية وزيادة شرب الماء فقط. تم توزيع 80 مريض بالغ يعانون من حصوات الكلى المتكررة على مجموعتين. شملت المجموعة الأولى 40 مريضًا تلقوا تعديلًا غذائيًا موحدًا وزيادة في شرب الماء فقط، بينما شملت المجموعة الثانية 40 مريضًا تلقوا أقراص سترات البوتاسيوم الفوارة (20 ملي مكافئ) مرتين يوميًا لمدة شهر، بالإضافة إلى نفس التعديل الغذائي الموحد وزيادة شرب الماء. وشملت التقييمات قياس المعايير البيوكيميائية في الدم والفحص بالموجات فوق الصوتية لعدد الحصوات وحجمها. وتم تصنيف الحصوات التي خرجت بشكل طبيعي خلال فترة الدراسة بشكل فيزيائي وتحليلها كيميائيًا باستخدام طريقة كيميائية نوعية/شبه كمية لتحديد تكوينها. انخفض عدد الحصوات بشكل كبير (p=0.030) في المجموعة 2 (0.60±0.71) مقارنة بالمجموعة 1 (1.90±3.60). أظهر تحليل الحصى أن حصوات أكسالات الكالسيوم كانت النوع السائد في كلتا المجموعتين، تلتها الحصوات التي تحتوي على حمض اليوريك. تم ملاحظة تحلل كامل للحصوات في 35% من المرضى في المجموعة 2 مقارنة بـ 0% في المجموعة 1، بينما كان تكون حصوات جديدة أقل تكرارًا في المجموعة 2. أظهرت النتائج الكيميائية الإحيائية والاشعاعية تفوق علاج سترات البوتاسيوم. أظهرت سترات البوتاسيوم تحسنات واعدة على المدى القصير، لكن هناك حاجة لدراسات عشوائية أكبر مع متابعة أطول.

الكلمات المفتاحية: حصوات الكلى، حصوة الكلى، منظف بول قلوي، سترات، إزالة الحصوة.

INTRODUCTION

Nephrolithiasis refers to kidney stone disease, demonstrating one of the oldest and most severe afflictions of the human urinary system [(1)]. While some stones stay asymptomatic and are only unintentionally diagnosed during imaging for unrelated conditions, they are presented as abdominal colic, an excruciating, paroxysmal pain[(2)]. Most stones are likely to pass with pharmacological therapy [(3)]. This recurrence inflicts a significant burden on patients, manifesting in recurrent events of tedious renal colic, anxiety, and uncertainty about future events, and the permanent need for expensive and invasive urological operations [(4)].

Kidney stone formation is a multifactorial, complicated process regulated by a physicochemical inequality: the urine starts supersaturated with stone-forming crystals such as calcium, oxalate, and uric acid [(5)]. This supersaturation is the thermodynamic driving force that promotes the nucleation, growth, sedimentation, and finally precipitation of crystalline sediment within the renal collecting tubules [(6)].

Among the pharmacological interventions suggested to mitigate this metabolic deficit, citrate-based therapy has become a gold standard for the treatment of recurrent kidney stones [(7)]. Citrate corrects the metabolic acidosis that is often the underlying cause of hypocitraturia [(8)]. Citrate increases urinary pH, stimulating renal tubular citrate reabsorption, leading to a marked increase in urinary citrate excretion [(9)]. This subsequent increase in urinary pH is valuable because it directly encourages the dissolution of uric acid, effectively blocking uric acid stone formation and the dissolution of present uric acid stones [(10)].

MATERIAL AND METHODS

Study setting: This randomized controlled prospective comparative interventional study was carried out among adult patients diagnosed with recurrent kidney stones who have visited the urology departments in Mosul Teaching Hospitals (Iraq). The study was conducted from November 19, 2025, to March 29, 2026, including patient recruitment, baseline evaluation, intervention, follow-up evaluation, laboratory investigations, ultrasound examination, stone analysis, and outcome recording.

Ethical approval: The study was conducted after obtaining ethical approval by the Pharmaceutical Research Ethics Committee in the College of Pharmacy (PREC-25-3-18 on 16 Nov 2025) and the Ninevah Health Directorate (Code 52489 on 20 Nov 2025). Consent form collected from participants. The patient's data sheet information was collected from each participant through a direct face-to-face interview using a structured patient data collection sheet.

Study design: Participants aged 18-65 years diagnosed with recurrent kidney stones were distributed into two comparative study groups. Patients were allocated to G1

(dietary modification and hydration alone) or G2 (potassium citrate therapy added to dietary modification and hydration) based on clinical indication. G2 patients had documented hypocitraturia (urinary citrate<320 mg/day), acidic urine (pH<5.5), or uric acid-containing stones, as per European Association of Urology (EAU) guidelines recommendations for citrate therapy (Figure 1). Allocation was determined through physician-patient shared decision-making. Laboratory personnel performing biochemical analyses were blinded to group allocation, though clinicians and patients were not blinded due to the nature of the intervention. The patients' adherence to therapy was followed up by continuous phone calls. Patients were advised to increase daily water intake, reduce excessive salt consumption, avoid excessive intake of animal protein, and maintain a balanced diet. They were also instructed to avoid dehydration and to distribute water intake throughout the day. They were also advised to avoid highly salted foods such as pickles, avoid excessive intake of spicy foods and condiments, and maintain a balanced diet.

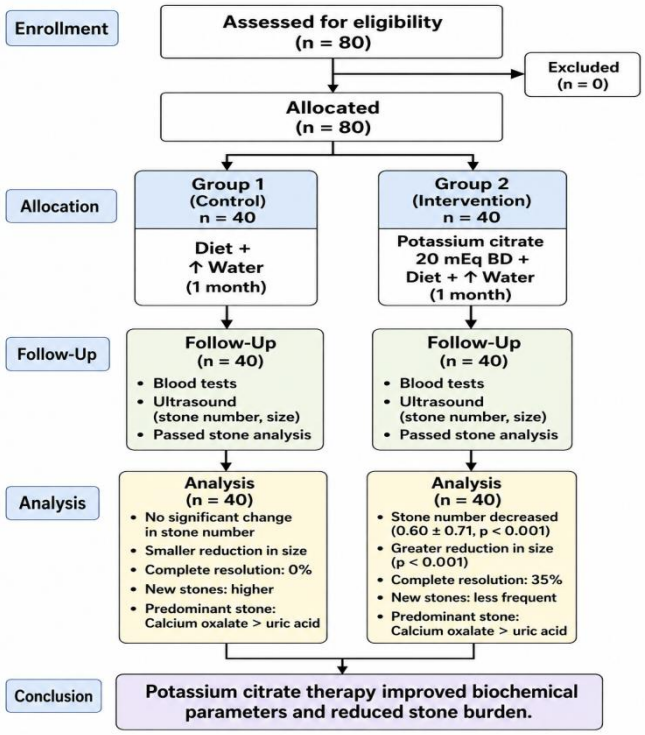

Figure (1): Flowchart of patient recruitment, treatment, and follow-up.

Duration of therapy and follow-up: The one-month follow-up duration was selected to capture early biochemical and stone burden changes in response to potassium citrate therapy, consistent with studies demonstrating that urinary alkalinization, citrate changes, and crystalluria resolution occur within weeks of initiating therapy [11]. We acknowledge that this duration is insufficient for assessing long-term stone recurrence rates, which require 6-12 months or longer of follow-up. Future studies with extended follow-up periods are recommended to evaluate sustained stone dissolution, recurrence prevention, and long-term renal function preservation.

Inclusion Criteria: Patients were included in the study if they fulfilled the following criteria:

- Adult patients aged 18-65 years.
- Patients diagnosed with recurrent kidney stones.
- Patients with a kidney stone confirmed by ultrasound examination.
- Patients willing to participate in the study and complete the one month of follow-up.
- Patients who provided informed consent before enrollment.
- Acidic urine pH.

Exclusion Criteria: Patients were excluded from the study if they had any of the following criteria:

- Age below 18 years or above 65 years.
- Pregnancy or lactation.
- Major systemic comorbidities that could interfere with biochemical parameters or stone-related outcomes such as hypertension, chronic kidney disease, or liver diseases.
- History of malignancy or a patient with active cancer.
- Drug-induced stones such as current alkalinising agents, diuretic therapy, or indinavir.
- Inability or non-compliance to complete the follow-up period.
- Incomplete baseline data that prevented valid statistical analysis.

Baseline assessment: At baseline, all patients underwent a standardized assessment using a structured patient data sheet. The baseline assessment included demographic data, anthropometric measurements, socio-occupational characteristics, clinical history, presenting complaints, stone history, family history of kidney stones, current stone characteristics, fluid intake, dietary risk factors, laboratory investigations, urine analysis, ultrasound examination, and stone-related evaluation. Demographic and socio-occupational data included age, sex, marital status, smoking status, residence or region, and relevant occupational or environmental exposure when present. Clinical assessment included the main presenting complaint and urinary symptoms, such as loin pain, incidental stone,

nausea, vomiting, dysuria, hematuria, intermittent urination, hesitancy, post-void dribbling, urinary retention, urgency, fever, frequency, and other relevant urinary complaints. Stone-related history included previous stone events, frequency of recurrence, time since the last stone episode, previous stone type when known, previous stone location and laterality, previous stone size and number, and history of prior urological intervention when applicable. Family history of kidney stone was recorded and classified according to first-degree and second-degree relatives. Current stone assessment included stone onset, renal location, number of stones, largest stone size and smallest stone size. Ultrasound examination was performed at baseline to confirm the presence of a kidney stone and to record stone number and stone size. Blood and urine samples were collected for biochemical assessment and urine analysis before starting the intervention.

Follow-Up assessment: All patients were reassessed after one month of follow-up. The same clinical, blood and urine biochemical, urine analysis, ultrasound, and stone-related parameters measured at baseline were repeated for both groups using the same devices and measurement methods. Follow-up assessment included evaluation of biochemical laboratory changes, urinary changes, stone number, largest stone size, smallest stone size, and stone-related clinical outcomes. These outcomes included stone reduction, stone increase, stone dissolution, stone passage, persistence of same stones or new stone formation, and need for intervention when applicable.

Blood sample collection: A total of 10 mL of venous blood was drawn from each patient by venipuncture; serum was separated from half and stored frozen at −20 °C until subsequent analysis. The other half was immediately analysed for specific parameters. This procedure was carried out at baseline and after one month of follow-up.

Stone sample collection: All patients enrolled in the study were advised to capture and retrieve any passed urinary stone during the study period whenever possible. Patients were instructed to place the stone on a clean, dry tissue; the retrieved stone was then received, dried completely, and placed in a dry container or tube. An identification label was affixed, including the patient code, the date and time of collection, and the date of one passage. The stones were subsequently analyzed in the laboratory using the semi-quantitative chemical method to determine their main chemical components, including calcium, oxalate, and uric acid.

Blood biochemical analysis: Blood urea was measured using the Mindray Urea Kit supplied by Shenzhen Mindray Bio-Medical Electronics. (China), based on the urease-glutamate dehydrogenase ultraviolet method. Serum creatinine was measured using the Mindray CREA-SOX Creatinine Kit supplied by Shenzhen Mindray Bio-Medical Electronics. (China), based on the sarcosine oxidase method [12]. Serum electrolytes, including potassium, sodium, chloride, ionized calcium, bicarbonate, and blood pH, were measured using the EXIAS e|1 electrolyte analyser and its corresponding multi-use cartridge system according to the manufacturer's instructions. Phosphorus concentration in the serum was determined quantitatively by a spectrophotometric method based on the ultraviolet phosphomolybdate method utilising the Mindray phosphorus kit supplied by Shenzhen Mindray Bio-Medical Electronics. (China). Serum uric acid was measured using the Mindray uric acid kit supplied by Shenzhen Mindray Bio-Medical Electronics (China), based on the uricase-peroxidase method.

The estimated glomerular filtration rate (eGFR) was calculated from serum creatinine values according to the following equation. eGFR was used as an estimated indicator of renal function in the studied groups [13].

$$\text{eGFR} = 142 \times \min\left(\frac{Scr}{\kappa}, 1\right)^{\alpha} \times \max\left(\frac{Scr}{\kappa}, 1\right)^{-1.200} \times 0.9938^{Age} \times [1.012 \text{ if female}]$$

Where:

- eGFR= estimated glomerular filtration rate (mL/min/1.73 m²)
- Scr= serum creatinine (mg/dL)
- κ (kappa)= 0.70 for females, 0.90 for males
- α (alpha)= −0.241 for females, −0.302 for males
- Age= years

Ultrasound measurement procedure: Ultrasound examination was used to confirm kidney stones and to assess stone burden at baseline and after one month of follow-up. The ultrasound parameters recorded in this study included the number of kidney stones, largest stone size in millimetres, and smallest stone size in millimetres. Ultrasound was conducted by radiologists in the radiology department of the hospital.

Kidney stone analysis: Kidney stone analysis was performed only when stones were retrieved from patients during the study period. Retrieved stones were collected, cleaned, dried and analyzed in the study laboratory according to standard laboratory practice.

Stone analysis included physical and chemical assessment. The physical assessment included the number of analyzed stones, shape, color, and size. The chemical analysis included detection of the main stone components, including calcium, oxalate, uric acid, phosphates, magnesium, ammonium, carbonate and cystine according to the kit instructions. Kidney stone composition was determined using the Biolabo stone analysis kit (REF 92315), employing ten specific reagents for the qualitative identification of eight major urinary calculi components, including carbonate, cystine, phosphate, magnesium, calcium, ammonium, uric acid, and oxalate, in accordance with the manufacturer's standardized protocol.

Sample size: Sample size was determined based on feasibility and consistency with published studies in the field. Comparable studies, including Barcelo et al.'s randomized trial (57 patients), demonstrated significant outcomes with similar or smaller sample sizes[14]. Post-hoc power analysis indicated that with 40 patients per group, the study had >80% power to detect the observed differences in primary outcomes (stone dissolution and urine pH change) at $\alpha = 0.05$ and a 95% confidence interval. Future studies with larger sample sizes and formal power calculations are recommended.

Statistical analysis: Data were entered, organized, coded, checked and arranged using Microsoft Excel 365 LTSC 2021, Version 2110, before statistical analysis. Continuous variables were expressed as mean±standard deviation (SD), whereas categorical variables were expressed as frequencies and percentages. Baseline and follow-up data were analysed for both study groups. Comparative analyses were performed using *IBM SPSS Statistics for Windows* (V26, USA). The normality of continuous variables was assessed before selecting the appropriate statistical tests using the Shapiro-Wilk test. For normally distributed variables, comparisons between the two independent study groups were performed using the independent samples t-test, whereas within-group comparisons between baseline and follow-up measurements were performed using the paired samples t-test. For non-normally distributed variables, the Mann-

Whitney U-test was used for between-group comparisons, and the Wilcoxon signed-rank test was used for within-group comparisons. Categorical variables were compared using the chi-square test or Fisher's exact test when appropriate. Statistical significance was considered at a p-value of less than 0.05.

RESULTS

Study population: A total of 80 participants with recurrent kidney stones were distributed into two study groups. Group 1 (G1) included 40 patients with recurrent kidney stones who were managed only with standardized dietary modification and increased water intake, whereas Group 2 (G2) included 40 patients with recurrent kidney stones who received potassium citrate therapy as a urinary alkalinising agent in addition to the same standardised dietary modification and increased water intake.

Demographic data of participants: Participants aged 40 years or younger represented 57.5% of G1, whereas those older than 40 years represented 60.0% of G2. Males predominated in both recurrent kidney stone groups, representing 72.5% of participants in both G1 and G2 (Table 1). The mean body mass index (BMI) was comparable between the two groups (28.52±6.31 kg/m² in G1, 28.28±5.13 kg/m² in G2). No statistically significant differences were observed between G1 and G2 regarding age category, sex distribution, BMI, marital status, or residence, indicating acceptable baseline demographic comparability between the two recurrent kidney stone study groups. A statistically significant difference was observed in the number of previous kidney stones: a single previous stone was more frequent in G1 (30 patients; 75.0%) compared with G2 (20 patients; 50.0%), whereas more than two stones were more common in G2 (20 patients; 50.0%) than in G1 (10 patients; 25.0%) (p=0.037).

Table (1): Demographic and Lifestyle characteristics of participants.

Variables		G1 n=40, n (%)	G2 n=40, n (%)	p-value
Age, years	≥40	17 (42.5)	24 (60.0)	0.179
	≤40	23 (57.5)	16 (40.0)	
Sex	Male	29 (72.5)	29 (72.5)	1.000
	Female	11 (27.5)	11 (27.5)	
BMI, kg/m2		28.52±6.31	28.28±5.13	0.851
Previous last stone number	1	30 (75.0)	20 (50.0)	**0.037**
	≥2	10 (25.0)	20 (50.0)	

Data are presented as n (%) unless otherwise stated. BMI= Body Mass Index is presented as mean±SD. The p-values refer to comparisons between G1 and G2. n: number of patients in each group. Using Chi-square and t-test for BMI.

Clinical data of participants: Loin pain was the most frequently reported clinical symptom among recurrent kidney stone patients, with the highest rate reported in G2 (n=34, 85.0%) (p=0.766), followed by G1 (n=32, 80.0%). Other symptoms were less frequently associated with the condition, including nausea, vomiting, dysuria, Hematuria, intermittent urination, post-void dribbling, urinary retention, and urgency (Table 2).

Table (2): Baseline Clinical Signs and Symptoms Among the Study Groups.

Clinical parameter	G1 n (%), n=40	G2 n (%), n=40	p-value
Loin pain	32 (80.0%)	34 (85.0%)	0.766
Incidental detection	6 (15.0%)	5 (12.5%)	1.000
Nausea	19 (47.5%)	16 (40.0%)	0.641
Vomiting	12 (30.0%)	13 (32.5%)	1.000
Dysuria	18 (45.0%)	17 (42.5%)	1.000
Hematuria at presentation	21 (52.5%)	16 (40.0%)	0.344
Intermittent urination	10 (25.0%)	12 (30.0%)	0.797
Post-void dribbling	11 (27.5%)	7 (17.5%)	0.424
Urinary retention	5 (12.5%)	2 (5.0%)	0.432
Urgency	12 (30.0%)	14 (35.0%)	0.812

Data are presented as frequency and percentage n (%). p-values refer to comparisons between G1 and G2 using Fisher's exact test. p-values are estimates pending confirmation from SPSS output. In the binary coding system, 1 indicates "Yes" and 0 indicates "No" for each recorded clinical parameter. The variable "incidental detection" was retained because some patients had urinary stones detected incidentally during clinical or imaging assessment without pain-related presentation.

Blood Parameters in the studied groups: Regarding blood biochemical parameters in G1, significant reductions were observed in blood urea and serum creatinine after one month of follow-up. Conversely, eGFR increased significantly. Serum chloride also increased significantly (p=0.005), serum phosphorus increased (p<0.001), and serum uric acid showed a small but significant increase from 4.43 to 4.71 mg/dL (p=0.042). Regarding G2, serum creatinine decreased significantly, while eGFR increased significantly. Serum phosphorus also increased. Blood urea decreased from 5.25 to 4.69 mmol/L; however, this change did not reach statistical significance (p=0.064). Other blood biochemical parameters in G2 showed no statistically significant changes (Figure 2).

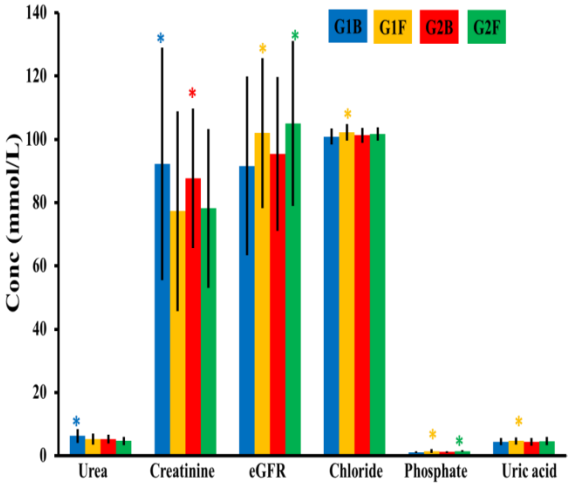

Figure (2): Concentration of measured blood parameters in the studied groups. The histogram bar and error bar represent mean±SD. The results demonstrated significant differences between groups at a p-value less than 0.05 using one-way ANOVA followed by post-hoc test at confidence intervals 95%. * Colour represents the significant difference when compared between baseline and follow-up. G1B= Baseline group 1, G1F= Follow-up group 1, G2B= Baseline group 2, G2F= Follow-up group 2.

Stone-related outcomes*:* Within-group changes in stone burden parameters from baseline to one-month follow-up are presented in Figure 3. In G1, stone number decreased slightly from 2.08±3.26 to 1.90±3.60; however, this reduction was not statistically significant (p=0.068). In contrast, the largest stone size showed a statistically significant reduction from 7.99±3.76 mm to 6.46±5.02 mm (p=0.001), whereas the reduction in the smallest stone size was not statistically significant (p=0.234). In G2, significant reductions were observed in all measured stone burden parameters. Stone number decreased from 3.25±8.01 to 0.60±0.71 (p<0.001), largest stone size decreased from 8.30±5.80 mm to 3.41±4.59 mm (p<0.001), and smallest stone size decreased from 1.87±3.47 mm to 0.97±2.90 mm (p=0.027). Within-group analysis demonstrated significant reductions in all three stone burden parameters in G2, whereas G1 showed a significant reduction only in the largest stone size.

Non-significant differences were observed between the two groups at baseline. After one month of follow-up, stone number was significantly lower in G2 compared with G1 (0.60±0.71 vs. 1.90±3.60, p=0.030). The mean largest stone size was also significantly lower in G2 than in G1 (3.41±4.59 mm vs. 6.46±5.02 mm, p=0.006). Although the mean smallest stone size was slightly lower in G2 compared with G1 (0.97±2.90 mm vs. 1.25±2.47 mm), this difference was not statistically significant (p=0.644). The between-group follow-up comparison showed statistically significant differences in both stone number and largest stone size, whereas the numerical difference in smallest stone size did not reach statistical significance.

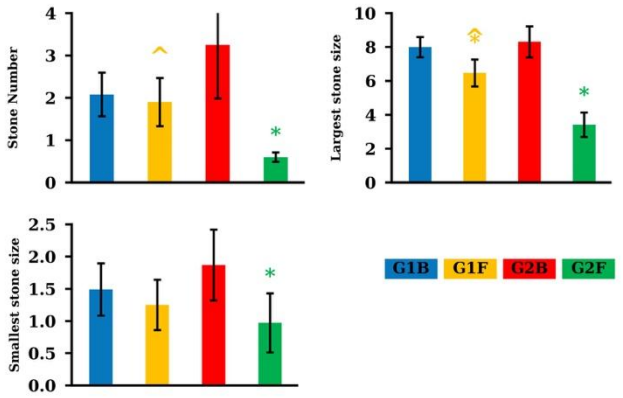

Figure (3): Stone burden parameters at baseline and after one month of follow-up in the studied groups. The histogram bar and error bar represent Mean±SEM. The results demonstrated significant differences between groups at a p-value less than 0.05 using one-way ANOVA followed by post-hoc test at confidence intervals 95%. * Colour represents the significant differences when compared between baseline and follow-up. ^ Comparison of follow-up groups. G1B= Baseline group 1, G1F= Follow-up group 1, G2B= Baseline group 2, G2F= Follow-up group 2.

Clinical stone outcomes after one month of follow-up among the study groups

Kidney stone size reduction after one month of follow-up was observed in 7 patients (17.5%) in G1 and 11 patients (27.5%) in G2. Kidney stone size increase after one month of follow-up was reported in 3 patients (7.5%) in G1 and 1 patient (2.5%) in G2. Kidney stone dissolution after one month of follow-up was not observed in G1, whereas it was recorded in 14 patients (35.0%) in G2. Spontaneous kidney stone passage at one-month follow-up was reported in 12 patients (30.0%) in G1 and 9 patients (22.5%) in G2. New kidney stone formation after one month of follow-up was observed in 4 patients (10.0%) in G1 and 1 patient (2.5%) in G2. The between-group comparison showed that kidney stone dissolution after one month of follow-up was significantly higher in G2 than in G1 (35.0% vs. 0.0%; Fisher's exact test $p<0.001$).

Although G2 showed a numerically higher proportion of kidney stone size reduction (27.5%) and lower proportions of kidney stone size increase (2.5%) and new kidney stone formation (2.5%) compared with G1, these differences were not significant. Therefore, these findings should be interpreted as a statistically significant between-group difference in kidney stone dissolution favoring G2 (35.0% vs. 0.0%; Fisher's exact test, $p<0.001$), whereas the remaining clinical stone outcomes showed only non-significant descriptive trends. Similarly, spontaneous kidney stone passage did not differ significantly between the two groups after one month of follow-up (Table 3).

Table (3): Clinical stone outcomes and urological interventions after one-month follow-up in G1 and G2.

Variables	Category	G1 (n=40) n (%)	G2 (n=40) n (%)	p-value
Kidney stone size decreased after one month of follow-up (cm)	No	33 (82.5%)	29 (72.5%)	0.422
	Yes	7 (17.5%)	11 (27.5%)	
Kidney stone size increased after one month of follow-up (cm)	No	37 (92.5%)	39 (97.5%)	0.615
	Yes	3 (7.5%)	1 (2.5%)	
Kidney stone dissolved after one month of follow-up	No	40 (100.0%)	26 (65.0%)	0.001
	Yes	0 (0.0%)	14 (35.0%)	
Kidney stone passage after one month of follow-up	No	28 (70.0%)	31 (77.5%)	0.612
	Yes	12 (30.0%)	9 (22.5%)	
New kidney stone formation after one month of follow-up	No	36 (90.0%)	39 (97.5%)	0.359
	Yes	4 (10.0%)	1 (2.5%)	

Data are presented as frequency and percentage, n (%). Between-group comparisons for binary outcomes were performed using Fisher's exact test. A p-value<0.05 was considered statistically significant.

Analysis of kidney stones passed during intervention in the studied groups.

With respect to chemical composition percentages, the analysis was performed only on retrieved stones, including 18 stones in G1 and 14 stones in G2. Uric acid, calcium, and oxalate were the only detected chemical components in the analyzed stones. In G1, the mean percentages of uric acid, calcium, and oxalate were 15.56±36.01%, 39.72±16.85%, and 44.72±21.45%, respectively. In G2, the corresponding values were 28.57±46.88%, 34.29±22.78%, and 37.14±24.63%, respectively.

Uric acid percentage was descriptively higher in G2 than in G1, whereas calcium and oxalate percentages were descriptively higher in G1 than in G2. However, Mann–Whitney U testing showed not statistically significant between-group differences in uric acid ($p=0.383$), calcium ($p=0.683$), or oxalate ($p=0.355$) composition percentages.

Carbonate, fibrin, cystine, ammonium, magnesium, phosphate, and urate salts were not detected in the analyzed stones of either group. Therefore, these components were reported as 0.00±0.00 in the descriptive analysis (Table 4).

Table (4): Semi-quantitative chemical composition analysis of kidney stones obtained during one month of follow-up study period.

Parameter	G1, n=18	G2, n=14	p-value
Carbonate (%)	0.00±0.00	0.00±0.00	---
Fibrin (%)	0.00±0.00	0.00±0.00	---
Cystine (%)	0.00±0.00	0.00±0.00	---
Ammonium (%)	0.00±0.00	0.00±0.00	---
Uric Acid (%)	15.56±36.01	28.57±46.88	0.383
Calcium (%)	39.72±16.85	34.29±22.78	0.683
Oxalate (%)	44.72±21.45	37.14±24.63	0.355
Magnesium (%)	0.00±0.00	0.00±0.00	---
Phosphate (%)	0.00±0.00	0.00±0.00	---
Urate Salts (%)	0.00±0.00	0.00±0.00	---
Data are presented as mean±standard deviation (SD). Chemical composition parameters are expressed as percentages. Between-group comparisons of chemical percentage parameters were performed using the Mann-Whitney U test. A p-value<0.05 was considered statistically significant. (0.00±0.00)=Not detected. Dashed lines indicate no comparison; negative result values. The analysis included 18 stones in G1 and 14 stones in G2.			

Urinary crystal type and retrieved kidney stone composition: The calcium oxalate stone composition was the predominant profile among retrieved stones in both study groups. In G1, 15 of 18 patients with available chemical analysis of retrieved stones (83.33%) had calcium oxalate stones, whereas 3 patients (16.67%) had uric acid stones. When baseline urinary crystal type was examined among G1 patients with calcium oxalate stones, amorphous urate crystal was the most frequent urinary crystal category, observed in 9 patients (50.00% of the G1 analyzed-stone subgroup). This was followed by no urinary crystal in 4 patients (22.22%) and calcium oxalate crystal in 2 patients (11.11%).

In G1, the 3 patients whose retrieved stones were classified as uric acid stones were all within the amorphous urate crystal category at baseline. This means that all uric acid stone cases in G1, within this cross-tabulated subgroup, had amorphous urate crystals at baseline.

In G2, calcium oxalate stone composition was also the most frequent retrieved stone profile. Specifically, 10 of 14 patients with available chemical analysis of retrieved stones (71.43%) had calcium oxalate stones, while 4 patients (28.57%) had uric acid stones. Among G2 patients with calcium oxalate stones, amorphous urate crystal at baseline was again the most frequent urinary crystal category, observed in 7 patients (50.00% of the G2 analyzed-stone subgroup). This was followed by calcium oxalate crystal in 2 patients (14.29%) and no urinary crystal in 1 patient (7.14%) (Table 5).

Table (5): Urinary crystal type and retrieved kidney stone composition for recurrent kidney stone patients.

Group	Urinary Crystal Type	Calcium oxalate stone n (%)	Uric acid stone n (%)
G1, n=18	No urinary crystal	4 (22.22%)	0 (0.00%)
	Calcium oxalate crystal	2 (11.11%)	0 (0.00%)
	Amorphous urate crystal	9 (50.00%)	3 (16.67%)
G2, n=14	No urinary crystal	1 (7.14%)	2 (14.29%)
	Calcium oxalate crystal	2 (14.29%)	0 (0.00%)
	Amorphous urate crystal	7 (50.00%)	2 (14.29%)
Values are expressed as frequency and percentage, n (%). Cases with unavailable stone composition analysis were excluded from this descriptive cross-tabulation. Stone composition was classified according to the dominant chemical profile as either a calcium oxalate stone or uric acid stone.			

DISCUSSION

The treatment of recurrent kidney stones managed with either standardized dietary modification and increased water intake with or without potassium citrate therapy demonstrated significant improvements in renal function parameters after one month of follow-up. In G1, serum creatinine decreased, with increased eGFR. This suggests that the renal function benefits of increased hydration are substantial and comparable across both groups[15]. A study in a rat model of polycystic kidney disease demonstrated that chronic potassium citrate/citric acid intake completely prevented the decline in glomerular filtration rate observed in untreated animals[16].

A notable finding was the significant increase in serum chloride in G1; increased water intake combined with reduced dietary sodium chloride consumption may lead to relative chloride retention. Improved hydration status and enhanced renal perfusion allow more effective tubular handling of electrolytes, with chloride being reabsorbed in proportion to sodium[17–19]. The absence of this change in G2 suggests that potassium citrate therapy modifies tubular electrolyte handling through its effects on acid-base balance[20]. This could be explained in the context of potassium citrate catabolised

to bicarbonate, producing a basic environment that increases urinary pH[21]. This alkaline milieu may jeopardise renal tubular ion exchange priorities, reducing net chloride reabsorption. Both groups increased serum phosphorus levels due to enhanced hydration expanding extracellular fluid volume, enhancing renal perfusion, subsequently increasing glomerular filtration, resulting in increased filtered phosphate load [22,23].

G1 demonstrated an increase in serum uric acid, which might reflect inflammatory responses associated with recurrent kidney stones. In G2, urinary alkalinization enhances uric acid dissolution and excretion. At pH 7.0, uric acid is completely ionised and highly soluble [10,24].

Serum calcium demonstrated no significant changes in either group. This stability is supportive, as calcium is a major participant in stone pathophysiology. Serum potassium demonstrated a slight increase in both groups. Despite the fact that potassium is part of citrate therapy, levels stayed within the normal range, which is congruent with the safety of potassium citrate [25]. Serum sodium showed no changes in either group, supporting that the therapy causes no marked electrolyte disturbances [19]. Blood pH remained stable in both groups, reflecting that the acid-base balance was preserved despite the alkalinising effect of citrate on urine [26]. This is consistent with citrate's primary action being on urinary, rather than systemic, pH.

Stone parameters, including stone number, largest stone size, or smallest stone size, have shown no notable differences at baseline in either group. Stone number decreased in both groups, with a marked reduction in G2 compared to the G1 group. This result is congruent with earlier studies, which demonstrated that potassium citrate therapy markedly reduced stone formation, with most of the treated patients achieving stone recurrence [27,28]. The reduction in stone number in G2 is consistent with the concept that citrate therapy alters the urinary milieu to perturb new stone formation and enhance the dissolution of existing lithos [4,29]. A study comparing potassium citrate with allopurinol plus potassium citrate demonstrated a decrease in stone size in both groups after therapy, with no significant difference in stone size change when the groups were compared [30], suggesting that potassium citrate alone is comparably efficacious for most patients with appropriate stone characteristics. Both groups have shown reductions in the largest stone size with a greater magnitude in G2. Consistent with this finding, an earlier study looking for oral citrate-based chemolysis for uric acid staghorn stones demonstrated that sufficient stone dissolution was achieved [31]. Similarly, both groups have shown reductions in the smallest stone size with greater magnitude in G2. Perhaps the smallest stone size was recently formed, favouring dissolution rather than stable stone formation [32,33].

The clinical features reflected that G2 offers a greater ratio of kidney stone dissolution, representing the most clinically meaningful difference between the two groups. Despite improved stone outcomes parameters (stone size reduction, stone size increase, spontaneous passage, and new stone formation) in G2, none reached significance upon follow-up. In line with this, a study looking for oral chemolysis for kidney stones demonstrated that urinary alkalinization by potassium citrate produced remarkable stone size reduction, regardless of allopurinol use [34]. Spontaneous kidney stone passage was reported in 12 patients (30.0%) in G1 and 9 patients (22.5%) in G2, with a non-significant difference($p=0.612$). This finding may contradict the general concept of citrate therapy. However, this could be explained in the context that stones in G2 were dissolved entirely rather than broken and passed as intact particles; the broken fragment is a case scenario with G1.

The stone analysis demonstrated that calcium oxalate was the commonest entity in retrieved stones in both groups, alongside uric acid presence in a large proportion of stones; other components of kidney stones were absent, including carbonate, fibrin, cystine, ammonium, magnesium, phosphate, and urate salts. This provides valuable data that help in the decision of treatment selection and preventive approaches. An earlier study confirmed that calcium oxalate accounts for up to 75% of all urinary stones [35]. A study analysed 3,789 kidney stones and demonstrated that calcium oxalate was present in up to 38.3% of stones [36]. Calcium oxalate stone formation starts with crystal formation and adhesion between crystals and tubular epithelial cells[24]**.** A German study of 45,783 urinary stones found that calcium oxalate was the most common main stone component, accounting for 71.4% of all stones. The EAU guidelines confirm that calcium oxalate monohydrate and dihydrate are the most common stone components [37]. The predominance of calcium oxalate stones in both groups has important clinical implications. Calcium oxalate is the most common stone type worldwide, and the recurrence rate among patients not taking potassium citrate is significantly higher than among those receiving citrate therapy [4,38].

The presence of uric acid in a large proportion of stones is clinically relevant because uric acid stones are responsive to citrate therapy [39]. Uric acid stones are associated with acidic urine pH (<5.5), and their solubility increases exponentially as urine pH rises above 6.0. The achievement of urine pH 7.0 in G2 in this study creates an environment highly favourable for uric acid dissolution[9], explaining the 35.0% stone dissolution rate observed in G2. Uric acid stones were more common in G2 than in G1, though this difference was not significant. This finding reflects the composition of stones retrieved from patients during the study period [40,41]. The presence of uric acid stones in both groups, and particularly the higher proportion in G2, suggests that patients with uric acid-containing stones may be more likely to respond to citrate therapy [8,22]. Uric acid stones are typically formed in highly acidic urine and account for approximately 8-10% of all urinary stones [22]. The solubility of uric acid increases exponentially as urine pH rises above 6.0; this explains the high dissolution rate observed in G2, where urine pH was increased from 5.7 to 7.0. The study of uric acid lithiasis found that patients in whom stones formed had significantly higher serum uric acid levels ($p<0.01$) associated with recurrent and/or bilateral stones [8]. This supports the use of alkalinization therapy for patients with uric acid stones.

Several limitations of the present study should be acknowledged. The one-month follow-up period is relatively short and may not be sufficient for the adaptation or the full therapeutic benefit of citrate therapy. The small sample size limits the generalizability of the findings. The stone composition was not comprehensively characterized, and intervention should be appropriately tailored to stone type, with citrate being particularly beneficial for uric acid stones and calcium oxalate stones with hypocitraturia. The evaluation of stone dissolution relied solely on imaging without direct stone retrieval and characterization of dissolution based on subjective investigation rather than normalized criteria.

CONCLUSION

Potassium citrate showed promising short-term improvements, but larger randomized studies with longer follow-up are needed**.** Citrate-based therapy was more effective than standardized dietary modification and increased water intake alone in improving urinary pH, slightly reducing lithogenic risk, and improving one-month stone outcomes in patients with recurrent kidney stones.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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