DIETARY PREDICTORS OF KIDNEY STONE RELAPSE AND COMPOSITION: ASSOCIATIONS WITH PASTA, MILK, AND ANIMAL PROTEIN INTAKE

Mihaela Nikolic[1], Roxana Lazăr[1], M. Ivănuță[2, 3], D. Ureche[4], M. N. Nicoară[5], Ramona-Alexandra Ciaușu[5*], Ancuța Andreea Miller[2], P. C. Boișteanu[1]

1. University of Life Sciences Ion Ionescu de la Brad Iasi, Romania
2. Grigore T. Popa University of Medicine and Pharmacy Iasi
3. Dr. C. I. Parhon Clinical Hospital, Iasi, Romania
4. Vasile Alecsandri University of Bacau
5. Alexandru Ioan Cuza University of Iasi / Doctoral School of Geosciences

[*]Corresponding author. E-mail: ciausuramona05@gmail.com

DIETARY PREDICTORS OF KIDNEY STONE RELAPSE AND COMPOSITION: ASSOCIATIONS WITH PASTA, MILK, AND ANIMAL PROTEIN INTAKE (Abstract): Dietary factors are known to influence the risk of nephrolithiasis recurrence, yet the specific contributions of refined carbohydrates (such as pasta), milk consumption (as a proxy for dietary calcium), and animal protein intake remain underexplored. **Materials and methods**: We analyzed data from 144 adult patients monitored between 2023 and 2025 at a clinical nutrition unit. Dietary exposures included weekly intake of pasta and milk (servings/week) and total animal protein (grams/week). The primary outcomes were lithiasis relapse (yes/no) and stone composition (calcium oxalate, uric acid, or mixed/other). Group comparisons were performed using the Mann-Whitney U or Kruskal-Wallis tests, followed by Benjamini-Hochberg False Discovery Rate (FDR) correction. Multivariate logistic regression was applied to identify independent dietary predictors of relapse and stone type, adjusting for age, sex, and residential environment. Random Forest models were used for exploratory prediction analyses. **Results**: Median pasta intake was higher among patients with relapse compared with non-relapsed individuals (1.0 vs 0.0 servings/week; $p = 0.012$). This association remained significant after FDR adjustment. Milk consumption differed significantly across stone types ($p = 0.013$; FDR-adjusted significant), with the highest values observed in calcium-oxalate stones. Animal protein intake showed a non-significant trend toward higher values in uric-acid stone formers. In multivariate analysis, pasta intake was an independent predictor of relapse, while milk and animal protein did not reach significance. The Random Forest models achieved modest predictive performance (accuracy = 0.53 for relapse; 0.68 for stone type classification). **Conclusions**: Higher pasta intake was independently associated with an increased risk of lithiasis relapse, and milk consumption differed by stone composition. These findings support the hypothesis that specific dietary patterns may influence nephrolithiasis outcomes, although the predictive value remains limited. Larger prospective studies are warranted to validate these associations and to refine personalized nutritional counselling strategies for stone prevention. **Keywords:** LITHIASIS, DIETARY FACTORS, PASTA INTAKE, MILK CONSUMPTION, ANIMAL PROTEIN, RELAPSE, KIDNEY STONES.

INTRODUCTION

Dietary and metabolic factors are recognized as crucial determinants of nephrolithiasis risk and recurrence (1-3). Despite advances in metabolic assessment and imaging, the incidence of lithiasis continues to rise globally, particularly among individuals with metabolic syndrome and type 2 diabetes mellitus (T2DM) (3, 7). This persistent increase underscores the need for a clearer understanding of modifiable nutritional contributors to stone formation.

Among dietary components, refined carbohydrates, dairy products, and animal protein have each been implicated in the complex metabolic mechanisms underlying lithogenesis (4-6, 8-11). Refined carbohydrate consumption, especially from pasta and starch-based foods, has been associated with insulin resistance, weight gain, and altered urinary excretion of calcium and oxalate (8). Conversely, milk provides dietary calcium that can reduce intestinal oxalate absorption but may simultaneously elevate urinary calcium concentrations (4, 9). High intake of animal protein contributes to an increased dietary acid load, lowering urinary pH and citrate levels while raising uric acid excretion, thereby promoting uric-acid stone formation (2, 10, 11).

However, few studies have simultaneously examined the relative contributions of these three key dietary elements—pasta, milk, and animal protein—to both lithiasis relapse and stone composition. Moreover, the available literature presents inconsistent findings, partly due to methodological heterogeneity and the limited integration of nutritional, metabolic, and predictive modeling approaches.

In this context, our study investigates the association between pasta intake, milk consumption, and animal protein intake with two major clinical outcomes: lithiasis relapse and stone composition. We further explore whether these dietary factors retain predictive value in multivariate models and in machine learning analyses. By focusing on specific, quantifiable dietary exposures within a well-characterized patient cohort, this research aims to clarify potential nutritional predictors of stone recurrence and composition, offering a basis for individualized dietary counseling and prevention strategies.

MATERIALS AND METHODS

This prospective observational study was conducted between 2023 and 2025 at a private nutrition and dietetics practice in Iași, Romania. The study enrolled patients diagnosed with obesity, type 2 diabetes mellitus (T2DM), and lithiasis, who met rigorous inclusion and exclusion criteria (12-17). All participants received detailed information about the study's objectives and procedures and provided written informed consent prior to enrollment, in accordance with ethical standards for human research. The study fully complied with the principles of the Declaration of Helsinki and received approval from the Institutional Ethics Committee (18).

Inclusion criteria required participants to be over 18 years of age, with a confirmed diagnosis of lithiasis documented through abdominal ultrasonography. Participants were also required to demonstrate the ability and willingness to attend all scheduled follow-up visits as outlined in the study protocol.

Exclusion criteria included the presence of acute complications, a current or past history of oncological disease, or contraindications to the imaging procedures used in the study (2, 19). Additional exclusion factors comprised pregnancy or breastfeeding, severe psychiatric disorders that could

interfere with protocol adherence, and refusal to participate.

Data collection involved participant screening and inclusion, obtaining informed consent, and collecting demographic and clinical information. Baseline anthropometric measurements were performed, medical documentation was reviewed, and participants completed standardized dietary behavior questionnaires (20).

The composition of kidney stones was determined by infrared spectroscopic analysis, performed at the Michel Daudon Center in Iași, which operates within the Urology Clinic of the Dr. C. I. Parhon Hospital, Iași. This method enabled precise identification of calcium oxalate, uric acid, and mixed stones, ensuring analytical consistency across all collected samples.

Statistical analysis was performed using R version 4.4.2. A significance level of $p < 0.05$ was adopted. Descriptive statistics were calculated for the cohort—means ± SD for continuous variables and counts (percentages) for categorical variables. For univariate comparisons between relapse groups, the Mann-Whitney U test was applied to continuous variables, and the Chi-square test was used for categorical variables. To compare continuous dietary variables across stone-type categories, the Kruskal-Wallis test was used.

To control for multiple testing across the dietary comparisons (three dietary factors × two outcomes), the Benjamini-Hochberg false discovery rate (FDR) procedure was applied. Multivariable logistic regression models were fitted with relapse (yes = 1, no = 0) as the dependent variable, and age, sex, urban residence (urban = 1), and the three dietary factors as independent predictors. Missing numeric values were imputed with cohort medians before regression analyses.

Secondary logistic regression models contrasted uric acid versus calcium oxalate stone composition as the outcome variable. For exploratory predictive modelling, we implemented Random Forest classifiers with stratified 70/30 train-test splits. Model performance was evaluated using overall accuracy and classification metrics computed on the held-out test set.

RESULTS

Between 2023 and 2025, a total of 867 individuals were evaluated at a private nutrition and dietetics practice in Iași, Romania, and 144 patients who met the eligibility criteria were included in the study. The mean age of participants was 52.25 ± 11.90 years. The sex distribution comprised 74 males (51.4%) and 70 females (48.6%). Regarding residence, 90 participants (62.5%) were from urban areas and 54 (37.5%) from rural areas.

Relapse status was available for 143 patients, and complete dietary information for the three factors (pasta, milk, and animal protein) was obtained for 142 patients. Complete data for both diet and relapse were available for 141 patients, as were datasets combining dietary and stone-type information.

Univariate analysis showed that patients who experienced relapse reported a higher pasta intake (median = 1.0 servings/week) compared with those without relapse (median = 0.0 servings/week), with a Mann-Whitney $p = 0.01225$.

Milk consumption did not differ significantly between relapse groups ($p= 0.32605$).

There was no significant association between animal-protein intake and relapse status: relapsed patients consumed a median of 110 g/week, whereas non-relapsed patients consumed 80 g/week (Mann-Whitney $p = 0.28031^{*}$) (tab. I).

No significant differences in demographic characteristics (age, sex, or urban versus rural residence) were observed between relapse and non-relapse groups.

Stone-composition analyses. Analysis by stone type (oxalate, uric acid, other) revealed significant variation in milk consumption, with calcium-oxalate stone formers showing the highest intake (Kruskal-Wallis p = 0.01260) (2, 9, 21).

Differences in animal-protein intake across stone-type groups approached statistical significance (p = 0.07928*), as uric-acid stone patients tended to consume more animal protein.

Pasta intake did not differ significantly between stone types (p = 0.14542*).

After applying the Benjamini-Hochberg false discovery rate (FDR) correction across the six dietary tests (three dietary factors × two outcomes), pasta consumption remained significantly associated with lithiasis relapse (adjusted p ≈ 0.0378).

Similarly, the association between milk consumption and stone type also remained significant (adjusted p ≈ 0.0378), confirming the robustness of both findings (tab. I).

Associations involving animal-protein intake lost statistical significance following FDR adjustment.

TABLE I

Univariate and multivariable analyses of dietary factors

Dietary factor	Relapse (median or trend)	P-value	Adjusted P-value (FDR)	Stone type (median or trend)	P-value	P-value (FDR)	Observations
Pasta (servings/week)	Relapse = 1.0; No relapse = 0.0	0.01225	0.0378	Oxalate = 0.5; Uric acid = 1.0; Other = 0.5	0.14542	-	Independent predictor of relapse
Milk consumption (per Serving / week)	-	0.32605	-	Higher in oxalate stones	0.01260	0.0378	Not significant for relapse
Animal protein (g/week)	Relapse = 110; No relapse = 80	0.28031	-	Oxalate = 90; Uric acid = 120; Other = 100	0.07928	-	Trend for uric acid stones, not significant after FDR

Multivariable logistic regression analyses, adjusted for age, sex, and urban residence, demonstrated that pasta consumption was an independent predictor of relapse. Neither animal protein nor milk intake were statistically significant predictors of relapse in the fully adjusted model.

A separate binary logistic regression comparing uric acid versus calcium oxalate stone composition revealed a positive association between animal protein intake and uric acid stones; however, this association lost statistical significance after application of the FDR correction (2, 10).

Additionally, the data indicated that patients with higher milk consumption tended to have elevated urinary calcium levels, which correlated with the formation of calcium-oxalate stones.

TABLE II
Predictive modeling with random forest

Outcome	Test Accuracy	Key Predictors	Observations
Relapse (binary)	0.53	Pasta intake	Model showed limited discrimination
Stone type (multiclass)	0.68	Milk intake	Moderate performance
Feature Importance	-	Pasta (relapse), Milk (stone type)	Consistent across models

The Random Forest classifiers trained with demographic and dietary information reached a 0.53 test accuracy for binary relapse prediction and 0.68 test accuracy for stone-type classification (multiclass outcome) based on the results (tab. II). The feature importance rankings showed that pasta and milk emerged as the leading predictors for their respective outcomes in both studies (7, 22).

DISCUSSION

This study demonstrates that specific eating habits-particularly pasta consumption, milk intake, and animal-protein consumption-are associated with the risk of lithiasis recurrence and stone composition. In a cohort of 144 patients, we identified a novel and statistically significant association between pasta intake and stone relapse, together with a robust relationship between milk consumption and stone composition (oxalate versus uric acid). Although animal-protein intake showed a biological tendency toward uric-acid stone development, this association did not remain statistically significant after FDR adjustment.

Our findings are consistent with the broader literature linking dietary patterns and nephrolithiasis. Dietary calcium derived from dairy products has repeatedly been shown to protect against calcium-oxalate stones in large cohorts and randomized clinical trials, primarily through intestinal binding of oxalate and the subsequent reduction in urinary oxalate excretion (4, 10, 23, 24). Therefore, the assessment and monitoring of active metabolic lithiasis must take these nutritional influences into account (12).

A high animal-protein intake is a classic risk factor for uric-acid lithiasis, increasing urinary acidity and urate excretion while reducing urinary citrate levels (2, 10, 11, 24). In our data, uric-acid stone formers tended to consume more animal protein; however, the limited sample size and semi-quantitative nature of dietary gram estimation likely reduced statistical power, leading to the loss of significance after FDR correction.

The association between pasta consumption and stone relapse represents an innovative signal of this study. Pasta, a refined carbohydrate with a high glycemic load, may contribute to lithogenesis through insulin resistance and associated changes in urinary uric acid and pH-mechanisms known to promote both uric-acid and mixed-type stone recurrence (3, 8, 13). While previous large-scale studies have investigated global dietary patterns and beverage types (25-27), very few have isolated pasta intake as an individual variable. Our findings suggest that frequent pasta consumption may serve as a proxy

marker for refined-carbohydrate, low-fiber dietary patterns associated with increased recurrence risk. Future mechanistic research should investigate whether pasta consumption directly alters urinary chemistry through metabolic effects.

The observed associations align with established biological pathways, which reinforces their physiological plausibility. Consumption of refined carbohydrates such as pasta induces postprandial hyperinsulinemia and, over time, insulin resistance, both of which influence urinary acidification and uric-acid metabolism. Milk provides calcium that binds intestinal oxalate, reducing its absorption, urinary oxalate concentration, and calcium-oxalate supersaturation (9,21). Population-based evidence further indicates that calcium-rich diets are associated with a lower recurrence risk across diverse populations (28). Conversely, animal-protein intake contributes to dietary acid load, lowering urinary citrate and increasing uric-acid excretion, thus fostering an environment conducive to uric-acid stone formation (2,10,11,24). The prevalence of oxalate lithiasis remains particularly influenced by environmental and dietary factors that modulate these metabolic pathways (2).

Our findings support the application of individualized dietary counseling in lithiasis management. Specifically, patients should be advised to (i) reduce refined-carbohydrate intake and favor low-glycemic, fiber-rich sources; (ii) obtain calcium primarily from milk and dairy products, rather than supplements consumed at inappropriate times; and (iii) moderate animal-protein intake, particularly in individuals prone to uric-acid stones. However, given the limited predictive power of diet-only models for relapse, comprehensive management should combine nutritional guidance with urinary biochemical monitoring and broader lifestyle interventions (24). Recent studies comparing type 1 and type 2 diabetic patients with nephrolithiasis underscore the necessity of tailoring management to metabolic profiles (7). Likewise, longitudinal assessments of renal function following nephrectomy highlight the long-term benefits of integrated dietary control on kidney health (17). Stone composition should therefore remain a central determinant in designing preventive and therapeutic strategies (6).

Despite the strengths of the present work, several limitations must be acknowledged. The observational and retrospective nature of the study precludes definitive causal inference and leaves room for residual confounding. The semi-quantitative dietary data introduce potential recall bias, and estimates of animal-protein intake (grams/week) may be imprecise. Although the overall cohort size provided adequate power to detect moderate associations, subgroup analyses by stone type were smaller and may have been underpowered. Finally, results from this single-cohort study may not be generalizable to populations with distinct dietary patterns, genetic backgrounds, or stone-formation rates.

CONCLUSIONS

In this cohort, pasta intake emerged as an FDR-significant correlate of stone relapse, while milk consumption was significantly associated with stone composition, showing patterns consistent with the protective physiology of calcium-oxalate stone formation. Animal-protein intake demonstrated a possible biological link with uric-

acid lithiasis, although statistical support was limited after adjustment.

Overall, these findings highlight that dietary factors alone cannot reliably predict stone recurrence, yet they identify promising avenues for further investigation into metabolic and dietary mechanisms underlying lithiasis. The results support the value of personalized nutrition counseling as an integral component of comprehensive stone-prevention strategies.

CONFLICT OF INTEREST AND FUNDING

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REFERENCES

1. Sima CS, Rascu ASC, Radavoi DG, *et al*. Profile of Common Nephrolithiasis Risk Variants in the Romanian Population. *Romanian J Urol* 2019; 18(4): 9-15.
2. Pricop C, Ivănuță M, Nikolic M, Puia D. Occurrence of human health risks of oxalate lithiasis generated by environmental and dietary factors. *Environ Eng Manag J* 2023; 22(5): 891-898.
3. Almuhanna NR, Alhussain AM, Aldamanhori RB, Alabdullah QA. Association of Chronic Hyperglycemia with the Risk of Urolithiasis. *Cureus* 2023; 15(10): e47385.
4. Curhan GC. Epidemiology of stone disease. *Urol Clin North Am* 2007; 34(3): 287-293.
5. Hughes P. Kidney stones epidemiology. Nephrology [Internet]. 2007 Feb [cited 2025 Oct 19]; 12(s1). Available from: https: //onlinelibrary.wiley.com/doi/10.1111/j.1440-1797. 2006. 00724.x
6. Ivanuta M, Puia D, Petrila O, Ivanuta AM, Pricop C. The Impact of Stone Composition on Treatment Strategies for Patients with Urolithiasis: A Narrative Review. *Cureus* [Internet]. 2024 Dec 8 [cited 2025 Oct 19]; Available from: https: //www.cureus.com/articles/323748-the-impact-of-stone-composition-on-treatment-strategies-for-patients-with-urolithiasis-a-narrative-review
7. Pricop C, Ivănuță M, Nikolic M, Puia D. Kidney Stones of Type I vs. Type II Diabetic Patients: Are There Any Differences? *J Clin Med* 2024; 13(20): 6110.
8. Barghouthy Y, Corrales M, Somani B. The Relationship between Modern Fad Diets and Kidney Stone Disease: A Systematic Review of Literature. *Nutrients* 2021; 13(12): 4270.
9. Taylor EN, Curhan GC. Dietary Calcium from Dairy and Nondairy Sources, and Risk of Symptomatic Kidney Stones. *J Urol* 2013; 190(4): 1255-1259.
10. Sorokin I, Mamoulakis C, Miyazawa K, Rodgers A, Talati J, Lotan Y. Epidemiology of stone disease across the world. *World J Urol* 2017; 35(9): 1301-1320.
11. Coe FL, Evan A, Worcester E. Kidney stone disease. *J Clin Invest* 2005; 115(10): 2598-2608.
12. Pricop C, Ivănuță M, Puia D. Active metabolic lithiasis: A condition that requires proper evaluation and monitoring. *Exp Ther Med* 2022; 24(6): 715.
13. Bray GA, Heisel WE, Afshin A, *et al*. The Science of Obesity Management: An Endocrine Society Scientific Statement. *Endocr Rev* 2018; 39(2): 79-132.
14. ElSayed NA, Aleppo G, Aroda VR, *et al*. Addendum. 2. Classification and Diagnosis of Diabetes: *Standards of Care in Diabetes-2023*. *Diabetes Care* 2023; 46(Suppl. 1): S19-S40. *Diabetes Care* 2023; 46(9): 1715-1715.

15. Marsden A, Shahtout A. International Organization for Standardization. In: Garcia LS, Allen TC, Baselski VS, Church DL, Karcher DS, Lewis MR, *et al*., editors. Clinical Laboratory Management [Internet]. 1st edition Wiley; 2024 [cited 2025 Oct 19]. p. 271-7. Available from: https://onlinelibrary.wiley.com/doi/10.1002/9781683673941.ch19
16. Lin BB, Lin ME, Huang RH, Hong YK, Lin BL, He XJ. Dietary and lifestyle factors for primary prevention of nephrolithiasis: a systematic review and meta-analysis. *BMC Nephrol* 2020; 21(1): 267.
17. Ivănuță M, Puia D, Cimpoeșu DC, Ivănuță AM, Bîcă OD, Pricop C. Longitudinal Evaluation of Renal Function in Patients with Acquired Solitary Kidney-Urological Perspectives Post-Nephrectomy. *J Clin Med* 2024; 13(23): 7470.
18. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *JAMA.* 2013; 310(20): 2191.
19. Dai JC, Pearle MS. Diet and Stone Disease in 2022. J Clin Med. 2022 Aug 13; 11(16): 4740.
20. D'Alessandro C, Ferraro PM, Cianchi C, Barsotti M, Gambaro G, Cupisti A. Which Diet for Calcium Stone Patients: A Real-World Approach to Preventive Care. *Nutrients* 2019; 11(5): 1182.
21. Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A Prospective Study of Dietary Calcium and Other Nutrients and the Risk of Symptomatic Kidney Stones. N Engl J Med. 1993 Mar 25; 328(12): 833-8.
22. Fan D, Liu H, Han Y, Gao Z, Gu Y. Machine learning algorithms for predicting stone residue and recurrence after lateral decubitus percutaneous nephrolithotomy. Medicine (Baltimore). 2025 Sept 19; 104(38): e44750.
23. Borghi L, Meschi T, Amato F, Briganti A, Novarini A, Giannini A. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. *J Urol* 1996; 155(3): 839-843.
24. Shah S, Calle JC. Dietary and medical management of recurrent nephrolithiasis. *Cleve Clin J Med* 2016; 83(6): 463-471.
25. Ferraro PM, Curhan GC, Gambaro G, Taylor EN. Total, Dietary, and Supplemental Vitamin C Intake and Risk of Incident Kidney Stones. *Am J Kidney Dis* 2016; 67(3): 400-407.
26. Ferraro PM, Taylor EN, Gambaro G, Curhan GC. Soda and Other Beverages and the Risk of Kidney Stones. *Clin J Am Soc Nephrol* 2013: 1389-1395.
27. Mahmoodi F, Andishgar A, Mahmoudi E, Monsef A, Bazmi S, Tabrizi R. Predicting symptomatic kidney stones using machine learning algorithms: insights from the Fasa adult's cohort study (FACS). *BMC Res Notes* 2024; 17(1): 318.
28. Cheraghian B, Meysam A, Hashemi SJ, *et al*. Kidney stones and dietary intake in adults: a population-based study in southwest Iran. *BMC Public Health* 2024; 24(1): 955.