International Surgery Journal
Wijayasuriya DSCR et al. Int Surg J. 2026 Jan;13(1):83-87
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20254102

Systematic Review

Prescribing acetazolamide and prevalence of nephrolithiasis: a systematic review

Don S. C. R. Wijayasuriya[1], Pinky T. M. Attale[2], Raashid M. Wani[3]*, Mudassir Wani[4]*

[1]Department of Urology, Aneurin Bevan University Health Board, Newport, UK
[2]Department of Emergency Medicine and Urgent Treatment Centre, Chelsea and Westminster Hospital, London, UK
[3]Department of Oculoplastic Surgery, Kashmir Eye Hospital, Kashmir, India
[4]Department of Urology, Cardiff, and Vale University Health Board, Cardiff, UK

Received: 02 November 2025
Revised: 05 December 2025
Accepted: 08 December 2025

***Correspondence:**
Dr. Raashid M. Wani,
E-mail: drmudds@gmail.com

ABSTRACT

Acetazolamide, a carbonic anhydrase inhibitor (CAI), is frequently prescribed for conditions such as idiopathic intracranial hypertension (IIH), glaucoma, and metabolic disorders. Despite its clinical efficacy, concerns have arisen regarding its potential to cause nephrolithiasis. This literature review examines existing evidence from peer-reviewed articles to determine how much acetazolamide contributes to kidney stone formation, exploring incidence rates, proposed mechanisms, and clinical considerations. Findings indicate that although there is an increased risk of calcium phosphate stone formation during acetazolamide treatment, especially in the early stages, this risk remains relatively low and is affected by patient-specific factors.

Keywords: Acetazolamide, Carbonic anhydrase inhibitor, Nephrolithiasis, Renal stones

INTRODUCTION

Nephrolithiasis, or renal stone disease, affects approximately 10-15% of the population in industrialised nations, with recurrence rates reaching up to 50% within the next decade.[1] It results from the saturation of urinary solutes, leading to crystal formation and aggregation within the renal collecting system, which in turn causes renal stones.[2] The majority of stones are composed of calcium salts. They are primarily calcium oxalate or calcium phosphate, although uric acid, cystine, and struvite stones are also present. A wide range of metabolic factors contribute to stone formation, including hypercalciuria, hypocitraturia, hyperoxaluria, and hyperuricosuria.[3] Urinary pH plays a key role in determining stone composition during daily clinical activities. While acidic urine favours uric acid stones, alkaline urine predisposes to calcium phosphate stones.[4] These metabolic abnormalities are seen primarily or secondarily to dietary factors, comorbidities (e.g. obesity, diabetes), or medications.[5]

Acetazolamide is a sulphonamide-derived CAI. It is commonly used in the treatment of a variety of causes, such as IIH, glaucoma, epilepsy, and acute mountain sickness. Acetazolamide acts primarily by inhibiting carbonic anhydrase in the proximal renal tubules, resulting in reduced bicarbonate reabsorption and the promotion of bicarbonate-rich diuresis.[6,7] This process leads to alkaline urine and metabolic acidosis, which in turn can influence a change in urinary biochemistry in a way that predisposes a person to renal stones.[6,7] Also, Acetazolamide has been shown to reduce urinary citrate levels, a key inhibitor of calcium crystal aggregation, and increase urinary calcium excretion, both of which facilitate calcium phosphate stone formation. The elevated urinary pH promotes the crystallisation of clinically significant calcium phosphate stones.[8,9]

This paper aims to review the existing literature on the relationship between acetazolamide use and the development of nephrolithiasis.

METHODS

We conducted a comprehensive literature search through our library services to identify relevant articles from January 1960 to March 2025. We searched PubMed, Embase, Medline, EBSCOhost, and Scopus databases for English-language articles using the following terms (Boolean operators: OR/AND used): "acetazolamide" OR "carbonic anhydrase inhibitor" AND "renal stone" OR "Nephrolithiasis". The title and abstract of each article were analysed, and relevant articles were identified for further review.

Inclusion criteria

We included peer-reviewed studies (case-control studies, cohort studies, retrospective analyses, and case series) that examined the relationship between acetazolamide or CAI use and nephrolithiasis development. Studies were required to report quantifiable outcomes such as incidence rates, risk factors, or temporal relationships between drug use and stone formation. Only English-language publications were included.

Exclusion criteria

We excluded narrative reviews without systematic methodology, editorials, letters to the editor, conference abstracts without full-text availability, case reports describing single patients, studies focusing on topical acetazolamide use only, studies with insufficient data on stone incidence or outcomes, and studies involving pediatric populations exclusively. Studies were also excluded if they did not clearly specify acetazolamide or CAI use as the primary exposure variable.

One hundred eleven articles matched initial search. After removing duplicates, 97 articles remained. Fifty-two were screened, after excluding 45 studies. Twenty-one full-text articles were assessed for inclusion. Using the SQR3 (Survey, question, read, recite and review) technique, 4 articles were included in final qualitative analysis.

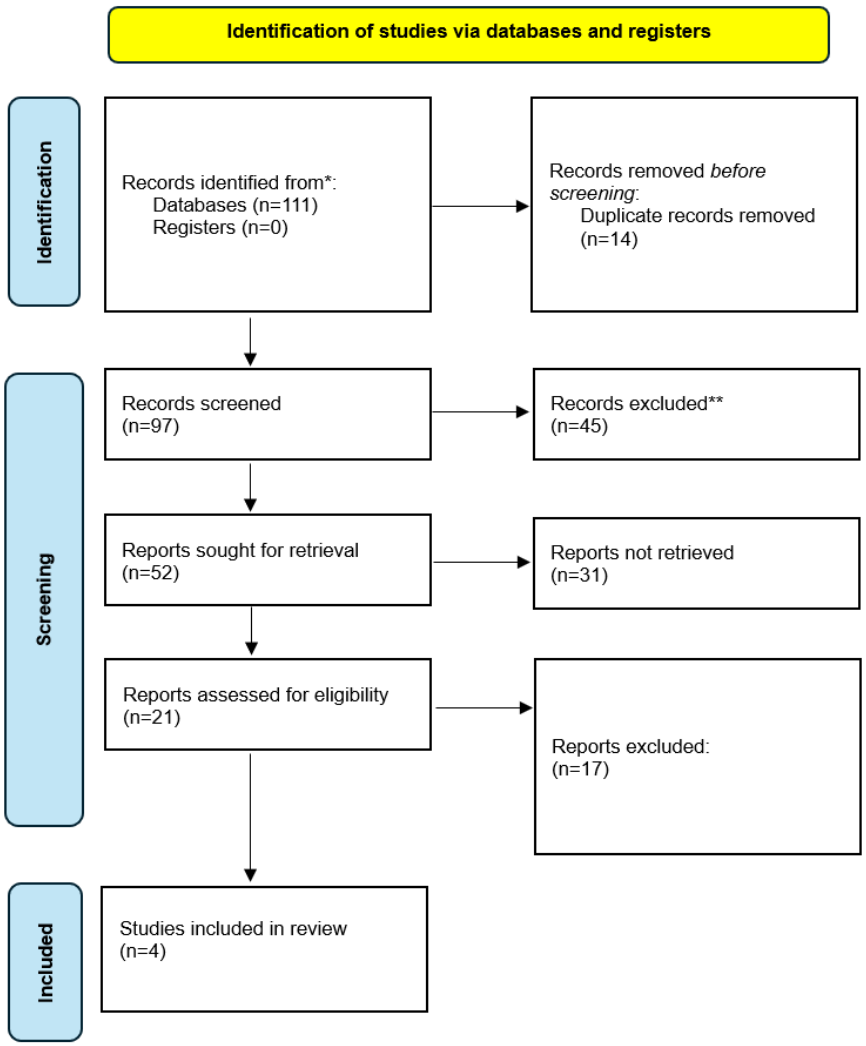

Figure 1: PRISMA chart.

RESULTS

The systematic literature search identified 111 articles across all databases. After removing 14 duplicates, 97 unique articles remained for screening. Title and abstract screening excluded 45 articles that did not meet the inclusion criteria, leaving 52 articles for detailed review. Following full-text assessment of 21 articles, 17 were excluded due to insufficient data on stone incidence (n=8), focus on topical use only (n=4), paediatric-only populations (n=3), and lack of clear acetazolamide exposure data (n=2). Ultimately, four articles met all inclusion criteria and were included in the final qualitative synthesis (Figure 1).

Four articles were included for the final literature review. The main features of the four articles are tabulated in Table 1.

The four included articles comprised two retrospective studies, one case-control study, and one review article, collectively examining the relationship between acetazolamide use and urolithiasis (Table 1). Kass et al conducted a retrospective interview-based study and concluded that chronic acetazolamide therapy is associated with increased occurrence of urolithiasis. Muayad et al performed a retrospective analysis specifically in patients with IIH treated with CAI s, identifying elevated kidney stone risk, particularly in male patients, while noting lower risk in Black/African American populations. Au et al conducted a case-control study examining daily acetazolamide use in the IIH population and reported that stone formation is relatively infrequent overall, but among those who develop stones, formation typically occurs within the first 18 months of treatment. Daudon et al provided a comprehensive review of drug-induced nephrolithiasis, highlighting that approximately 10% of acetazolamide-treated patients develop stones, with a higher risk in those with pre-existing urolithiasis or hypercalciuria.

The results from the articles are summarised in the Table 2.

Clinical and demographic characteristics across the four studies revealed important variations in study populations and outcomes (Table 2). Sample sizes ranged from 47 patients in the case-control study (Au et al) to 4,422 patients in the large retrospective cohort (Muayad et al). The studies reported varying incidence rates of nephrolithiasis: Kass et al reported 11% stone development among chronic acetazolamide users compared to less than 1% in controls; Muayad et al documented an overall incidence rate of 0.73% in IIH patients on CAIs; and Au et al found a 6.5% incidence among long-term acetazolamide users, and Daudon et al. review reported a 10% incidence rate. The median time to stone formation, where reported, was 13.1 months (Au et al). All studies focused on patients with specific indications for acetazolamide use, including glaucoma, IIH, and other conditions requiring chronic CAI therapy.[10-12]

Table 1: Demographic characteristics of articles.

Study	Aim	Type	Main outcome
Kass et al[10]	This study evaluated chronic acetazolamide use and the incidence of urolithiasis	Retrospective study (Interview-based)	The results of this study support the clinical impression that chronic acetazolamide therapy is associated with an increased occurrence of urolithiasis
Mauyad et al[11]	This study evaluates the risk of kidney stone development in patients with IIH treated with CAIs	Retrospective study	CAI use in patients with IIH may increase kidney stone risk, particularly in certain populations. Higher risk in the male population and lower risk in the black/ African American population
Au et al[12]	This study examined daily acetazolamide use and its relationship to nephrolithiasis	Case-control study	This study concluded 1) Stone formation during acetazolamide treatment is a relatively infrequent occurrence within the IIH population. 2) Among patients who develop a stone, formation is likely to occur within 1 year and a half. 3) There is no evidence to support the association between acetazolamide daily dosage and stone development
Daudon et al[13]	This study includes drug-induced nephrolithiasis and crystalline nephropathy	Review	Drug-induced nephrolithiasis is mainly due to two reasons: poorly soluble drugs with high urine excretion that favour the crystallisation of urine, and drugs provoking the formation of stones as a consequence of metabolic effects

Table 2: Results and outcomes of the articles.

Studies	Methodology	Main outcomes	Remarks
Kass et al[10]	Interviews were conducted with 515 individuals to look for the incidence of urolithiasis in patients treated for ophthalmological conditions. 148 were treated with chronic oral acetazolamide therapy for one week to 348 months	12 patients developed one or more stones during acetazolamide therapy, 9 out of 12 developed within the first year of treatment. The rate of individuals developing 1 or more stones per year during acetazolamide treatment was 11 times higher than rate in group not treated with acetazolamide	The results of this study support the clinical impression that chronic acetazolamide therapy is associated with an increased occurrence of urolithiasis
Mauyad et al[11]	Comparison of patients receiving treatment for IIH with CAI (Acetazolamide, methazolamide), to those who did not receive CAI. CAI group-23,182 patients, non-CAI group-50,080 patients	Comparison of kidney stone risk in treated vs. untreated patients with IIH, 1 year-1.49, 2 year-2.24 and 3 year-1.51	Higher risk in men
Au et al[12]	Out of 670 patients receiving treatment using Acetazolamide, 19 patients (2.8%) developed nephrolithiasis; out of these, 17 patients (89.5%) developed stones within 1.5 years of initial acetazolamide therapy	This study concluded that daily acetazolamide was not significantly associated with stone formation. Also, the relationship between the clinical presentation of IIH at the time of diagnosis and stone development did not reach statistical significance.	Patients with IIH receiving acetazolamide should be monitored for stone development, especially within 1st year and a half of treatment
Daudon et al[13]	Review article analysing drug-induced kidney stones and crystalline nephropathy	10% of patients receiving Acetazolamide develop nephrolithiasis. A history of urolithiasis or underlying hypercalciuria is associated with a higher risk of stone formation in patients receiving CAI treatment	Topical treatment of Acetazolamide is less likely to lead to nephrolithiasis

DISCUSSION

CAI are used in the treatment of glaucoma and serve as an adjunct in managing IIH, some forms of epilepsy, or post-hemorrhagic hydrocephalus in newborns.[12,14,15] Acetazolamide or its analogues, such as methazolamide, ethoxzolamide, and dichlorphenamide, target different isoforms of carbonic anhydrase in ocular tissue. However, similar mechanisms lead to systemic adverse effects. In the kidneys, CAI act on the proximal convoluted tubule, blocking bicarbonate reabsorption and inhibiting the excretion of hydrogen ions, which results in intracellular acidosis and increased tubular reabsorption of citrate ions, leading to hypocitraturia.[16,17] Major lithogenic factors in patients treated with acetazolamide include profound hypocitraturia, elevated urine pH, and hypercalciuria.[18] In these patients, urine composition favours the precipitation of calcium phosphate, mainly in the form of carbapatite.[19]

The first documented association between CAI and nephrolithiasis was in 1954.[20] The estimated incidence is approximately 10%.[21] Although not all users will develop stones, certain individuals who already have existing metabolic predispositions may be at an increased risk when using acetazolamide within the first 18 months.[10,13]

This review indicates that patients on chronic acetazolamide treatment face an increased risk of nephrolithiasis. This risk is greater during the first two years of treatment.[10-12] The relationship between CAI dose and the occurrence of nephrolithiasis is not clear; some articles suggest a link while others find no association.[11,12] However, topical treatment has not been associated with urolithiasis.[13] Individual susceptibility to stone formation seems to be influenced by underlying metabolic conditions and gender.[11] This literature review advises vigilant monitoring for urolithiasis rather than discontinuation, especially for patients who benefit significantly from acetazolamide therapy.

This literature review has many limitations. There is a scarcity of literature available, and additionally, there is a lot of variability in reported incidence may be attributable to differences in study design, population characteristics, and duration of follow-up.

The main goal of this literature is to help clinicians in making informed decisions regarding the risk-benefit profile of chronic acetazolamide use for different medical conditions.

CONCLUSION

Acetazolamide use is associated with a quantifiable increase in risk of renal stone formation. Although overall incidence remains low, the risk is clinically relevant and warrants routine monitoring. Future studies should aim to better stratify risk, assess effectiveness of prophylactic measures and clarify dose-related relationships.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Rule AD, Lieske JC, Li X, Melton LJ, Krambeck AE, Bergstralh EJ. The ROKS nomogram for predicting a second symptomatic stone episode. J Am Society Nephrol. 2014;25(12):2878-86.
2. Khan SR. Reactive oxygen species, inflammation and calcium oxalate nephrolithiasis. Translat Androl Urol. 2013;3(3):256-76.
3. Curhan GC. Epidemiology of stone disease. Urologic Clin N Am. 2007;34(3):287-93.
4. Coe FL, Evan A, Worcester E. Kidney stone disease. J Clin Investigat. 2005;115(10):2598-608.
5. 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):1301-20.
6. Daudon M, Jungers P. Drug-induced renal calculi: epidemiology, prevention and management. Drugs. 2004;64(3):245-75.
7. Elkinton JR, Huth EJ, Webster GD Jr, McCance RA. The renal excretion of hydrogen ion in renal tubular acidosis. I. quantitative assessment of the response to ammonium chloride as an acid load. Am J Med. 1960;29:554-75.
8. Constant MA, Becker B. The effect of carbonic anhydrase inhibitors on urinary excretion of citrate by humans. Am J Ophthalmol. 1960;49:929-34.
9. Awuah Boadi E, Shin S, Yeroushalmi S, Choi BE, Li P, Bandyopadhyay BC. Modulation of Tubular pH by Acetazolamide in a Ca^{2+} Transport Deficient Mice Facilitates Calcium Nephrolithiasis. Int J Mol Sci. 2021;22(6):3050.
10. Kass MA, Kolker AE, Gordon M. Acetazolamide and urolithiasis. Ophthalmology. 1981;88(3):261-5.
11. Muayad J, Alryalat SA, Al Deyabat O, Loya A, Lee AG. Assessing the Risk of Kidney Stone Development in Patients with Idiopathic Intracranial Hypertension Treated with Carbonic Anhydrase Inhibitors. J Neuroophthalmol. 2024;45(4):420-5.
12. Au JN, Waslo CS, McGwin G Jr, Huisingh C, Tanne E. Acetazolamide-Induced Nephrolithiasis in Idiopathic Intracranial Hypertension Patients. J Neuroophthalmol. 2016;36(2):126-30.
13. Daudon M, Frochot V, Bazin D, Jungers P. Drug-Induced Kidney Stones and Crystalline Nephropathy: Pathophysiology, Prevention and Treatment. Drugs. 2018;78(2):163-201.
14. Katayama F, Miura H, Takanashi S. Long-term effectiveness and side effects of acetazolamide as an adjunct to other anticonvulsants in the treatment of refractory epilepsies. Brain Dev. 2002;24(3):150-4.
15. Libenson MH, Kaye EM, Rosman NP, Gilmore HE. Acetazolamide and furosemide for posthemorrhagic hydrocephalus of the newborn. Pediatr Neurol. 1999;20(3):185-91.
16. Parfitt AM. Acetazolamide and sodium bicarbonate induced nephrocalcinosis and nephrolithiasis; relationship to citrate and calcium excretion. Arch Intern Med. 1969;124(6):736-40.
17. Higashihara E, Nutahara K, Takeuchi T, Shoji N, Araie M, Aso Y. Calcium metabolism in acidotic patients induced by carbonic anhydrase inhibitors: responses to citrate. J Urol. 1991;145(5):942-8.
18. Parikh JR, Nolan RL. Acetazolamide-induced nephrocalcinosis. Abdom Imaging. 1994;19(5):466-7.
19. Paisley KE, Tomson CR. Calcium phosphate stones during long-term acetazolamide treatment for epilepsy. Postgrad Med J. 1999;75(885):427-8.
20. Persky L, Chambers D, Potts A. Calculus formation and ureteral colic following acetazolamide (Diamox) therapy. J Am Med Assoc. 1956;161(17):1625-6.
21. Resor SR Jr, Resor LD. Chronic acetazolamide monotherapy in the treatment of juvenile myoclonic epilepsy. Neurology. 1990;40(11):1677-81.

Cite this article as: Wijayasuriya DSCR, Attale PTM, Wani RM, Wani M. Prescribing acetazolamide and prevalence of nephrolithiasis: a systematic review. Int Surg J 2026;13:83-7.