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Role of Antacids in Kidney Stone Formation: A Systematic Review

Khaled Hamed, Rawan Saeed, Mahmoud Bakaria, Betül Sadeddin

Citation 1 change
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REVIEW TITLE AND BASIC DETAILS

Review title
Role of Antacids in Kidney Stone Formation: A Systematic Review

Condition or domain being studied
Kidney Stone; Nephrolithiasis; Uric Acid Renal Calculus; Ureteric Stone; Uric Acid Crystalluria; Crystalluria; Urinary Crystal, Calcium Sulfate; Matrix Stone Of Kidney

This review will examine the relationship between exposure to antacids (including calcium-, magnesium-, and aluminum-containing compounds) and the development of kidney stones or urinary crystal formation in humans. Both clinical outcomes and experimental evidence (in vitro or animal studies) will be included.

Rationale for the review
Antacids, including calcium-, magnesium-, and aluminum-containing compounds, are widely used for gastrointestinal disorders. Some components, particularly calcium and magnesium, may alter urinary composition, pH, and solubility, potentially promoting the nucleation, growth, and aggregation of crystals in the urinary tract, leading to kidney stone formation. Although isolated clinical case reports and experimental studies suggest a link, no comprehensive synthesis exists. This systematic review aims to collate and critically appraise both clinical and experimental evidence on the role of antacids in kidney stone formation. By synthesizing current knowledge, the review will clarify the potential risk associated with antacid use, identify gaps in the literature, and provide guidance for clinicians regarding the safety and monitoring of patients using these agents. It may also inform future research directions on mechanisms of drug-induced nephrolithiasis.

Review objectives

To systematically evaluate the evidence on how exposure to antacids, including calcium-, magnesium-, and aluminum-containing compounds, affects the risk of kidney stone formation in humans. Specifically, the review aims to:

1. Assess the incidence of kidney stone formation associated with antacid use.
2. Examine the types and composition of stones formed in antacid users.
3. Evaluate changes in urinary parameters, such as pH and crystalluria, linked to antacid exposure.
4. Synthesize experimental evidence from in vitro and animal studies on the mechanisms of crystal nucleation, growth, and aggregation induced by antacids.

Keywords

Antacids; Kidney stones; Nephrolithiasis; Crystalluria ; Magnesium Hydroxide

Country

Türkiye

ELIGIBILITY CRITERIA

Population

Included

Humans (adults and children) exposed to any type of antacid for any indication, at any dose or duration.

Excluded

Studies not involving human subjects for clinical outcomes (e.g., purely in vitro or animal studies will be included only in the experimental evidence synthesis).

Intervention(s) or exposure(s)

Included

Antacid; Calcium Carbonate; Magnesium Hydroxide; Aluminium Hydroxide; Alginic Acid / Magnesium Carbonate Oral Suspension

Ingestion of antacids, including but not limited to:

1. Calcium carbonate
2. Magnesium hydroxide
3. Aluminum hydroxide
4. Magnesium trisilicate
5. Combination antacid products
6. All doses, durations, and indications are included.

Excluded

- Interventions not classified as antacids (e.g., proton pump inhibitors, H2-receptor antagonists)
- Studies without clear documentation of antacid exposure for clinical outcomes

Comparator(s) or control(s)

Included
PICO tags selected: Placebo; H2-receptor Antagonists; Proton pump inhibitor

Comparators can include individuals who have not taken antacids or who are receiving other medications for similar indications. A comparator is not required for case reports, case series, or experimental studies.

Excluded
Studies comparing different types of antacids without a non-antacid or placebo group (unless mechanistic experimental studies are included)

Study design
Both randomized and nonrandomized study types will be included.

Included

- Randomised studies: Randomized controlled trials (RCTs) evaluating the effect of antacids on kidney stone formation or urinary crystallization.
- Non-randomised studies: Cohort studies, case-control studies, cross-sectional studies, case reports, and case series.
- Experimental studies: In vitro crystallization assays and animal studies will be included to provide mechanistic insights and will be synthesized narratively.

Excluded

- Studies not involving humans for clinical outcomes (except experimental studies included for mechanistic purposes).
- Studies evaluating medications other than antacids without relevant exposure data.
- Reviews, editorials, or commentaries without original data.

Context
This review will include studies conducted in any healthcare or community setting worldwide, including hospitals, outpatient clinics, and general population cohorts. There are no geographic restrictions. Both clinical and experimental studies will be considered, with experimental studies conducted in laboratories or animal facilities included to provide mechanistic insights. The context is defined broadly to capture all relevant evidence on the impact of antacids on kidney stone formation.

TIMELINE OF THE REVIEW

Date of first submission to PROSPERO
29 August 2025

Review timeline 1 change
Start date: 1 September 2025. End date: 30 October 2025.

Date of registration in PROSPERO

29 August 2025

AVAILABILITY OF FULL PROTOCOL

Availability of full protocol

A full protocol has been written and uploaded to PROSPERO. The protocol may be accessed through this link https://www.crd.york.ac.uk/PROSPEROFILES/cd7fb8c3ba31e6fdddb456eee0b06794.pdf.

SEARCHING AND SCREENING

Search for unpublished studies

Both published and unpublished studies will be sought.

Main bibliographic databases that will be searched

The main databases to be searched are *CENTRAL - Cochrane Central Register of Controlled Trials*, *CLIB - The Cochrane Library*, *Embase - Embase via Ovid*, *Embase.com*, *MEDLINE*, *PubMed* and *Scopus*.

Search language restrictions

There are no language restrictions.

Search date restrictions

There are no search date restrictions.

Other methods of identifying studies

Other studies will be identified by: *contacting authors or experts*, *looking through all the articles that cite the papers included in the review ("snowballing")*, *reference list checking*, *searching conference proceedings* and *searching trial or study registers*.

Additional information about identifying studies

Additional studies will be identified through expert consultation, citation tracking, conference abstracts, and clinical trial registries to ensure comprehensive coverage of published and unpublished evidence.

Link to search strategy

A full search strategy is available in the full protocol as described in the *Availability of full protocol* section

Selection process

Studies will be screened independently by at least two people (or person/machine combination) with a process to resolve differences.

Other relevant information about searching and screening

Reference management software (e.g., EndNote or Zotero) will be used to import search results and remove duplicates. Titles and abstracts will be screened first, followed by full-text assessment according to predefined eligibility criteria. Disagreements will be resolved by discussion, and if

necessary, a third reviewer will arbitrate. A PRISMA flow diagram will be used to document the study selection process.

DATA COLLECTION PROCESS

Data extraction from published articles and reports

Data will be extracted by one person (or a machine) and checked by at least one other person (or machine).

Authors will be asked to provide any required data not available in published reports.

Study risk of bias or quality assessment

Risk of bias will be assessed using: *Cochrane RoB-1*, *Newcastle-Ottawa*

Joanna Briggs Institute (JBI) Critical Appraisal Checklist (for case reports and case series)

Narrative quality assessment (for in vitro and animal studies, since standardized risk of bias tools do not fully apply)

Data will be assessed independently by at least two people (or person/machine combination) with a process to resolve differences.

Additional information will be sought from study investigators if required information is unclear or unavailable in the study publications/reports.

Reporting bias assessment

We will assess risk of bias due to missing results using funnel plot asymmetry (if ≥10 studies are available) and Egger's test where appropriate. Selective reporting will be evaluated against study protocols/registries when available. Narrative assessment will be provided for smaller evidence bases.

Certainty assessment

Certainty of findings will be assessed using the GRADE approach for clinical outcomes, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. For observational and experimental studies, certainty will be appraised narratively, and overall confidence in evidence will be transparently reported.

OUTCOMES TO BE ANALYSED

Main outcomes

The primary outcome will be the incidence and prevalence of kidney stone formation associated with antacid use, as confirmed by imaging, clinical diagnosis, or stone passage. Effect measures will include risk ratios, odds ratios, or hazard ratios where available. Acceptable measurement methods include radiological imaging, laboratory-confirmed stone composition, and medical records. Time points will include both short-term and long-term follow-up, as reported in each study.

Additional outcomes

Secondary outcomes will include: (1) type and composition of kidney stones (e.g., calcium oxalate, calcium phosphate, uric acid) confirmed by laboratory analysis; (2) urinary biochemical changes (e.g., urinary calcium, oxalate, citrate, pH) measured by standard laboratory methods; (3) recurrence of kidney stones during follow-up, reported as incidence or time-to-event; (4) adverse events or side effects associated with long-term antacid use; and (5) healthcare utilization related to kidney stone management, including hospitalizations, emergency visits, or surgical interventions. Effect measures will be extracted as reported in primary studies (e.g., mean difference, relative risk, hazard ratio).

PLANNED DATA SYNTHESIS

Strategy for data synthesis

Formal synthesis is planned. Where studies are sufficiently homogeneous in terms of population, intervention, and outcomes, quantitative synthesis will be conducted using meta-analysis. Relative risks (RR), odds ratios (OR), or hazard ratios (HR) will be pooled for dichotomous outcomes, while mean differences (MD) or standardized mean differences (SMD) with 95% confidence intervals will be calculated for continuous outcomes. A random-effects model will be applied given the expected clinical and methodological heterogeneity. Statistical heterogeneity will be assessed using the I^2 statistic and Chi^2 test. If quantitative synthesis is not appropriate, results will be summarized narratively, structured around type of antacid, population characteristics, and outcome measures. Subgroup analyses will be considered where data permit (e.g., by age, sex, type of antacid, or baseline stone risk).

CURRENT REVIEW STAGE

Stage of the review at this submission 1 change

Review stage	Started	Completed
Pilot work	✓	✓
Formal searching/study identification	✓	✓
Screening search results against inclusion criteria	✓	✓
Data extraction or receipt of IPD	✓	✓
Risk of bias/quality assessment	✓	✓
Data synthesis	✓	

Review status

The review is currently planned or ongoing.

Publication of review results

Results of the review will be published in English and Turkish.

REVIEW AFFILIATION, FUNDING AND PEER REVIEW

Review team members 1 change

Khaled Hamed (review guarantor and contact) ORCID: 0000-0003-1716-9382. Ondokuz Mayız University. Türkiye.

No conflict of interest declared.

Rawan Saeed. Ondokuz Mayız University. Türkiye.

No conflict of interest declared.

Mahmoud Bakaria. Ondokuz Mayız University. Türkiye.

No conflict of interest declared.

Betül Sadeddin. Ondokuz Mayız University. Türkiye.

No conflict of interest declared.

Named contact

Khaled Hamed (khaled.gamal1a@med.svu.edu.eg). ORCID: 0000-0003-1716-9382. Ondokuz Mayız University. Türkiye.

Review affiliation

Ondokuz Mayıs University, Turkey

Funding source

Review has no specific/external funding but is supported by guarantor/review team (non-commercial) institutions.

Additional information about funding

This review is conducted as part of the guarantor's academic work and supported by Ondokuz Mayıs University; no commercial funding has been received

Peer review

There has been no peer review of this planned review.

ADDITIONAL INFORMATION

Additional information

This systematic review aims to synthesize clinical and experimental evidence on the role of commonly used antacids in kidney stone formation. It includes both human and mechanistic studies to provide a comprehensive understanding of the potential risk, stone composition, and underlying mechanisms. The review will inform clinicians and patients about possible adverse effects of long-term or high-dose antacid use, and identify gaps in current research for future studies.

Review conflict of interest

Declared individual interests are recorded under team member details.. No additional interests are recorded for this review.

Medical Subject Headings

Kidney Calculi; Urolithiasis; Urinary Calculi; Aluminum Hydroxide; Antacids; Magnesium Hydroxide; Calcium Carbonate

Revision note 1 change

I am adding details of the Review Team

SIMILAR REVIEWS

Check for similar records already in PROSPERO

PROSPERO identified a number of existing PROSPERO records that were similar to this one (last check made on 29 August 2025). These are shown below along with the reasons given by that the review team for the reviews being different and/or proceeding.

- The Association Between Carbonated Soft Drink Consumption and Risk of Calcium Oxalate Renal Calculi in Adults: A Systematic Review [published 29 July 2025] [CRD420251115721]. The review was judged **not to be similar**
- A Systematic review of gene polymorphisms predisposing to urinary tract calcium [published 9 February 2022] [CRD42022301692]. The review was judged **not to be similar**
- A Systematic review of gene polymorphisms predisposing to urinary tract calcium stones [published 5 February 2022] [CRD42022250427]. The review was judged **not to be similar**

PROSPERO version history 1 change

- Version 2.0, published 22 Oct 2025
- Version 1.0, published 29 Aug 2025

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