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Acute Kidney Injury and NSAID Use: A Systematic Review and Meta-analysis

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Background

Acute kidney injury (AKI) is a clinically serious adverse event associated with nonsteroidal anti-inflammatory drug (NSAID) use and represents an important concern for patient safety and public health.

Objective

To quantify the association between NSAID exposure and AKI among community-dwelling adults.

Study Design

A systematic review and meta-analysis.

Methods

A comprehensive literature search was conducted in PubMed, Embase, the Cochrane Library, Scopus, and Web of Science for studies published up to October 7, 2025. Adjusted odds ratios (aORs) were pooled using a generic inverse-variance method across predefined NSAID exposure windows, including current use, prescription ending within 1-30 days, 31-365 days before the AKI event; and dispensing-based exposure within 0–30 days and 1–90 days before the AKI event. The certainty of the evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.

Results

Nine studies were included, with seven pooled in the meta-analysis and two synthesized narratively. Individuals with AKI were associated with significantly higher odds of current NSAID use compared with non-AKI individuals (OR, 1.77; 95% confidence interval [CI], 1.17–2.67). No significant association was observed between NSAID use and AKI when prescriptions had ended 1–30 or 31–365 days before the AKI event. In contrast, AKI cases had significantly higher odds of recent NSAID dispensing, particularly within 0–30 days (OR, 2.44; 95% CI, 1.35–4.40), and 1–90 days (OR, 1.81; 95% CI, 1.36–2.41) before the AKI event. According to the GRADE framework, the certainty of evidence for all outcomes was rated as very low.

Limitations

The available evidence was limited, given heterogeneity among the included studies with respect to study design, populations, AKI definitions, and exposure characterization. In addition, limited data and inconsistent exposure definitions precluded stratified analyses by individual NSAIDs or high-risk subgroups.

Conclusion

NSAID use and AKI appear to be associated, particularly for NSAID current use and recent dispensing within 0-30 and 1–90 days before the AKI event.

First author, year	Study design	Data source	Study population	Exclusion criteria	Case-control definition	Index date definition	NSAID exposure definition	AKI definition	Number of participants (n)	Adjusted effect estimates (aOR, 95% CI)	Adjusted covariates
Chou et al (31) 2016	Nested case–control	Taiwan's National Health Insurance Research Database (NHIRD), 1,000,000 pers on Longitudinal Health Insurance Data base (LHID) subset	Taiwanese adults ≥ 20 years	History of CKD (ICD-9-CM) or kidney transplantation	**Case:** Participants with AK I according to established criteria **Control:** ≤1 matched by age, sex, and month and year of cohort entry, without AKI	Date of hospital admission for AKI	Oral NSAID prescriptions issued within 1 year before the index date, classified as: Current: AKI occurring during active NSAID prescription; Recent: 1–30 days after the prescription end; Past: 31–180 days after prescription end	Based on ICD-9-CM code 584.9	n=30995 (Case: n=6199; Control: n=24796)	Current: 2.73 (2.28–3.28); Recent (1–30 days): 1.17 (1.01–1.35); Past (31–180 days): 0.62 (0.55–0.70)	Age, sex, monthly income, urbanization, Charlson Comorbidity Index, AKI risk factors, concomitant medications, and other comorbidities.
Evans et al (22) 1995	Case–control	Medicines Monitoring Unit's (MEMO) record linkage database, Scotland	residents of Tayside (=420, 600 individuals) registered with a GP in May 1990	Not explicitly reported	**Case:** Participants with AKI according to the established criteria between January 1, 1990, and December 31, 1992 **Control:** 6:1 matched by sex, age, index date, alive as of September 1992	Date of first hospital admission for AKI after January 1, 1990	Prior oral NSAIDs, topical NSAIDs, and dispensed aspirin, classified as: Recent: ≥ 1 prescription dispensed within 90 days before the index date; Previous: ≥ 1 prescription dispensed from January 1989 to the index date	ICD-9 code for AKI, validated by ≥ 20% decline or ≥ 20% post treatment improvement in renal function	n=144) (Case: n=207; Control: n=1238)	Recent oral NSAIDs: 2.20 (1.49–3.25)	Age, sex; additional confounders not reported.
Griffin et al (23) 2000	Nested case–control	Tennessee Medicaid data base	Tennessee Medicaid enrollees aged >65 years with ≥ 1 year of continuous enrollment before the index date; residents of 19 remote counties were excluded	ESRD, hospital-acquired AKI, missing or poor quality data, stable CKD, probable stable chronic renal insufficiency, AKI unrelated to NSAID	**Case:** Participants with AKI according to the established criteria **Control:** Participants with out AKI	Date of first hospital admission for AKI	Non-aspirin NSAIDs, based on prescription, classified as: Current: AKI diagnosed during active prescription; Recent: 1–30 days after prescription end; Past: 31–365 days after prescription end; Nonuse: no NSAID prescriptions in the 365 days before the index date	Cr > 180 μmol/L with ≥ 20% increase from baseline or ≥ 20% decline during hospitalization.	n=11698 (Case: n=1799); Control: n=9899)	Current: 1.58 (1.34–1.86); Recent (1–30 days): 0.84 (0.55–1.27); Past (31–365 days): 0.87 (0.74–1.01)	Age, sex, ethnicity, nursing home residence, recent hospitalization, drugs within the past 30 days, prescription for allopurinol, cyclosporin, gold, sulfinpyrazone, or penicillamine, first prescription for cimetidine within the past 60 days, and exposure to IV radiocontrast within the past 30 days.
Pérez Gutthann et al (24) 1996	Nested case–control	Linked administrative health databases from the Saskatchewan Department of Health, Canada	Saskatchewan residents with ≥1 NSAID prescription (1982–1986), continuously enrolled in the provincial health plan	Malignant neoplasms, CKD, (>hospital-onset of AKI, missing data, or other renal/systemic diseases	**Case:** Participants with AK I according to the established criteria **Control:** Randomly selected cohort members without prior renal disease or malignancy and free of AKI at the index date	Date of hospital admission for AKI	NSAIDs prescriptions based on the dispensing date of the mo st recent prescription, classified as: Current: 0–30 days before the index date; Recent: 31–60 days before the index date; Past: 61–150 days before the index date; Nonuse: no prescription in the 150 days before the index date	Hospital discharge diagnosis of AKI or renal failure, recent onset of uremia, oliguria, or anuri a, Cr > 150 μmol/L (1.7 mg/dL), BUN > 1/ mmol/L (47.6 mg/dL) or serum urea > 10 mmol/L (28 mg/dL), with no renal disorders or systemic disease	n=2035 (Case: n=28; Control: n=1997)	Current: 4.10 (1.50–10.80); Recent: 0.80 (0.20–4.11); Past: 1.50 (0.40–5.6)	Age, sex, calendar year, cardiovascular risk marker, recent non-renal hospitalization, NSAID use, prescription aspirin, and nephrotoxic drug use.
Huerta et al (25) 2005	Nested case–control	General Practice Research Database (GPRD), United Kingdom	Adults aged 50 –84 years, registered with a GP for 2 2 years, with ≥ 1 year of computerized prescription history.	Cancer, renal disor der , cirrhosis, systemic connective tissue disease, age ≥70 year s, fewer than two health contacts during follow up	**Case:** Participants with AKI according to the established criteria **Control:** Random cohort members, matched by index date, age, sex, and calendar year.	Date of first diagnosis of AKI	NSAID use is classified as: Current: 0–30 days ending before the index date; Recent: 31–365 days ending before the index date; Past: ending > 1 year before the index date; Nonuse: no prior record	Clinically specialist-confirmed AKI with serum Cr > 1.7 mg/dL (150 mol/L) or serum urea > 47.6 (17.0 mmol/L) mg/dL, and no exclusion criteria.	n=5103 (Case: n=103; Control: n=5000)	Current (0–30 days): 3.23 (1.79–5.82); Recent (31–365 days): 1.71 (0.88–3.33) ; Past (> 365 days): 1.26 (0.74–2.14)	Sex, age, calendar year, body mass index, heart failure, hypertension, diabetes, use of antihypertensives, oral steroid use, NSAID exposure, and healthcare utilization in the past year.
Leonard et al (26) 2012	Retrospective case–control	General Practice Research Database (GPRD), United Kingdom	Not reported	History of kidney transplant; occurrence of AKI or AIN, within the 180-day baseline period	**Case:** Participants with AKI according to the estab lished criteria **Control:** Up to 50 controls per case selected by incidence density sampling, matched on sex, age, and index date.	Date of first diagnosis of AKI	Active traditional NSAID on index date (drug supply based)	based on diagnostic codes	n=151832 (Case: n=27982; Control: n=1123850)	1.31 (1.22–1.37)	Recent hospitalization (within 90 days); prior history of anemia, vascular diseases, hypertension, esophageal disorders, gastrointestinal disorders, arthropathies, dorsopathies, non-back rheumatism, pain conditions, pneumonia, viral or chlamydial diseases, mental health disorders; previous use of medications for gastrointestinal, endocrine, hematologic conditions, malignancy or immunosuppression; amiodarin use within 10 days; exposure to kidney-sensitizing drugs within 180 days before the index date.
Nash et al (27) 2019	Retrospective cohort study	Institute for Cli nical Evaluative Sciences (ICES) – Linked Heal h Administrati ve Databases, Ontario, Canad a	Adults aged ≥ 65 years residing within the laboratory catchment area	Age: 65–66 years, prior NSAID use within 6 months, recent hospital discharge ≤2 days, missing baseline Cr or K+ within the prior year, baseline K+ > 5.5 mmol/L or potassium binder use in the past 6 months, eGFR >150 ml /min/ 1.73 m^2, residence outside laboratory catchment area, ESRD, or (for non-users) no healthcare encounter within 30 days	Not a case control study (cohort design); Participants are classified into NSAID users vs. non-users	Date of NSAID was dispensed (NSAID user)	Prescription based NSAID use: > 1 prescription for an NSAID with > 14-day supply; Follow-up: 30 days after the index date	Serum Cr increase of ≥ 50% from baseline or > 0.3 mg/dl. (26.5 μmol/l) within 30 days after the index date	n=92714 (NSAID users: n=46107; NSAID nonusers: n=46107)	1.43 (1.20–1.65)	Propensity score matching based on >150 baseline variables, including demographics; index prescription characteristics; prescribing physician characteristics; health care visits in prior year; comorbidities (past 5 years); healthcare utilization and laboratory testing (prior year); and medication use (120 days before the index date)
Schneider et al (28) 2006	Nested case–control	Databases of t he universal he alth program f or residents of Quebec, Cana da	Resident aged ≥ 65 years, with ≥ 1 NSAID description between January 1, 1999, and June 30, 2002, who were NSAID-free for ≥1 year before cohort entry	Aspirin-only users; non-aspirin NSAID use in prior year; underwent renal replacement therapy or kidney transplantation, or ≥ 2 NSAIDs on the same day at cohort entry	**Case:** Participants with the first AKI according to the established criteria **Control:** Up to 20 controls matched to cases on age, month/year of cohort entry	Date of hospital admission with AKI	NSAIDs prescriptions in the 365 days before the index date, classified based on the dispensing dates: Current: 1–30 days before the index date; Recent: 31–90 days before the index date; Past: 91–365 days before the index date	Based on ICD-9 diagnosis codes.	n=87958 (Case: n=4228; Control: n=83510)	Current (1–30 days): 2.05 (1.61 –2.60); Current and recent (1–90 days): 1.62 (1.29–2.04); Current continuous use: (1–365 days): 1.14 (1.01–1.28); Recent use (31–90 days): 0.96 (0.85–1.08); Past use (91–365 days): 0.77 (0.69–0.85)	Age, sex, comorbidity, drug use , current aspirin use, use of nephrotoxic drugs, exposure to contrast media, comorbidity measures, and health care utilization
Wang et al (29) 2024	Case-crossover	Taiwan National Health Insurance Research Data base (NHIRD), Longitudinal Health Insurance Database (LHID)	Participants with the first AKI according to the established criteria	Any outpatient visits or hospitalization for CKD within 365 days before the index date	**Case period:** 1–7 days before the first hospitalization date due to AKI. **Control period:** 181–187 days before the index date	Date of first admission of AKI	Active NSAID use (case–control periods): Dispensed prescription (based on calculated days-supply) covering 1–7 days before the index date (case period); Control period: 181–187 days before the index date (180 days apart)	Based on ICD-9-CM codes	n=1394	NSAIDs use (1–7 days): 3.71 (2.62 –5.25); NSAIDs use (8–14 days): 1.47 (1.12–1.94); NSAIDs use (15–30 days): 1.27 (0. 99–1.62); NSAIDs use: (8–30 days): 1.43 (1.13–1.80); NSAIDs use (31–90 days): 1.22 (0.97–1.55)	Discordant comorbidities and concomitant medications between the case period (1–180 days) and control period (181–360 days).

Table 1. Characteristics of the included studies

Figure 1. Meta-analysis of the association between NSAID use and AKI, stratified by specific exposure windows.

Outcome	Number of included Studies	Risk of bias[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Publication bias[e]	Factors to rate up	Summary of findings			
								Pooled OR (95% CI)	Number of participants	Level of evidence	Importance
Current NSAID use	3	No	Very serious (-2)	Serious (-1)	No	Not assessed	No	1.77 (1.17–2.67)	1394525	Very low	Critical
NSAID prescriptions ending 1-30 days before AKI events	2	No	Serious (-1)	Serious (-1)	Serious (-1)	Not assessed	No	1.05 (0.78–1.42)	42693	Very low	Critical
NSAID prescriptions ending 31-365 days before AKI events	2	No	Very serious (-2)	Serious (-1)	Serious (-1)	Not assessed	No	1.13 (0.59–2.14)	16801	Very low	Critical
Prescriptions dispensing within 0-30 days compared to the AKI events	2	No	Serious (-1)	Serious (-1)	No	Not assessed	No	2.44 (1.35–4.40)	90783	Very low	Critical
Prescriptions dispensing within 1-90 days compared to the AKI events	2	No	Serious (-1)	Serious (-1)	No	Not assessed	No	1.81 (1.36–2.41)	90213	Very low	Critical

Table 3. Assessment of evidence certainty according to the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach.