Nephrotoxicity Profiles of Commonly Prescribed Antibiotics in Hospitalized Adult Inpatients: A Pharmacovigilance Cohort Across Tertiary Wards with Multivariable Risk Analysis

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***Abstract*—Acute kidney injury attributable to antibiotic exposure is a frequent yet frequently overlooked adverse event in hospital inpatients. We conducted a prospective pharmacovigilance cohort study across general medical, surgical, and intensive care wards at a tertiary hospital, enrolling 315 adult patients receiving antibiotics with documented nephrotoxic potential over 14 months. AKI by KDIGO criteria occurred in 68 patients (21.6%), with stage 1 in 41 (13.0%), stage 2 in 19 (6.0%), and stage 3 in 8 (2.5%). Incidence varied substantially by exposure: 14.3% with vancomycin alone, 27.8% with vancomycin and piperacillin-tazobactam in combination, 23.6% with aminoglycosides, and 38.5% with colistin. The risk gradient across baseline eGFR strata was steep, with combined exposures yielding AKI in over 40% of patients with baseline eGFR below 30. The strongest independent predictors were severe baseline renal impairment (adjusted HR 7.85), hypotension during exposure (HR 3.84), multiple concurrent nephrotoxin exposure (HR 3.18), and concurrent contrast administration (HR 2.42). Renal recovery to baseline at 60 days occurred in 92% of stage 1, 68% of stage 2, and 38% of stage 3 cases. The findings reinforce the case for structured renal-aware antimicrobial stewardship with dose-adjustment algorithms, hypotension surveillance, and avoidance of preventable combination exposures.**

***Index Terms*—antibiotic nephrotoxicity, acute kidney injury, vancomycin, piperacillin-tazobactam, aminoglycosides, colistin, pharmacovigilance, antimicrobial stewardship**

I. Introduction

Hospital-acquired acute kidney injury substantially increases length of stay, in-hospital mortality, and the risk of progression to chronic kidney disease. Among its many causes, drug-induced injury is one of the most frequent and the most modifiable. Antibiotics — used in a majority of hospital admissions in some form, often in combination, often at full doses during the period of highest physiological stress — account for a substantial fraction of drug-induced AKI episodes. Yet the specific contribution of individual antibiotic classes, the interaction between baseline renal function and exposure, and the contribution of co-administered nephrotoxins remain incompletely characterised in many practice settings. Several lines of evidence have raised concern about specific antibiotic combinations in particular. Vancomycin and piperacillin-tazobactam given together a common combination for empirical coverage of healthcare-associated infections have been associated with substantially higher AKI rates than either agent alone. Aminoglycoside nephrotoxicity is a long-recognised concern that has been mitigated but not eliminated by once-daily dosing and therapeutic drug monitoring. Colistin and polymyxin B, increasingly used for multidrug-resistant gram-negative infections, retain a nephrotoxicity profile from the original studies in the 1960s with only modest modification despite renewed clinical interest (Jha, Kumar,, & Neha, 2026; Bhatnagar, Kumar,, & Shivam, 2026). We undertook a prospective pharmacovigilance cohort study to characterise AKI incidence across antibiotic classes in a real-world tertiary setting, to identify independent risk factors that might inform structured stewardship algorithms, to examine recovery trajectories across AKI severity strata, and to document the operational gap between optimal renal-aware prescribing and observed practice (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Yatish, Khatoon,, & Kumar, 2026).

II. Methods

The study was conducted across general medical, general surgical, and intensive care wards at a tertiary teaching hospital between February 2023 and March 2024. Adult inpatients (age ≥18) prescribed any antibiotic from the predefined nephrotoxic-potential list vancomycin, piperacillin-tazobactam, aminoglycosides, colistin or polymyxin B, conventional or lipid-formulation amphotericin B, cefepime, or linezolid for at least 48 hours were eligible. Patients on chronic renal replacement therapy at the time of exposure, those with kidney transplant within 90 days, and those with admission creatinine values unavailable were excluded. The final cohort comprised 315 patients with adequate creatinine surveillance data. Antibiotic exposures were tracked through the institutional pharmacy dispensing system with verification against the nursing administration record. Concurrent exposure was defined as overlap of at least 24 hours between two or more nephrotoxic agents. The pre-specified combination of interest was vancomycin and piperacillin-tazobactam, given the prior literature suggesting an interaction beyond simple additivity. Total duration of exposure, peak daily dose, and where applicable therapeutic drug monitoring trough values were recorded. Serum creatinine was measured at baseline (within 48 hours before exposure initiation), daily for the first 72 hours of exposure, every 48 hours thereafter while on therapy, and at day 7, 14, 30, and 60 after exposure completion. AKI was defined and staged using KDIGO 2012 criteria: stage 1 (creatinine rise ≥0.3 mg/dL within 48 hours or 1.5-1.9× baseline within 7 days), stage 2 (2.0-2.9× baseline), or stage 3 (≥3.0× baseline, absolute value ≥4.0 mg/dL, or initiation of renal replacement therapy). Cases were adjudicated by a nephrologist blinded to exposure category to address alternative aetiology (sepsis, contrast, hypovolaemia, obstruction). Primary outcomes were AKI incidence overall and by exposure category, and identification of independent risk factors through multivariable Cox regression. Secondary outcomes included AKI severity distribution, time to AKI onset, requirement for renal replacement therapy, renal recovery trajectory, length of stay, and in-hospital mortality. Recovery was categorised at day 60 as complete (creatinine within 10% of baseline), partial, or persistent. Continuous variables are summarised by median and interquartile range. Comparisons used chi-squared and log-rank tests as appropriate, with multivariable adjustment for clinically prespecified covariates.

III. Results

3.1 Cohort and Exposure Characteristics

Table 1. Baseline characteristics of the study cohort (n=315).

Characteristic	All patients (n=315)	AKI cases (n=68)	No AKI (n=247)
Age, mean (SD), years	62.4 (16.2)	68.8 (14.4)	60.6 (16.4)
Age ≥65, n (%)	146 (46.3)	42 (61.8)	104 (42.1)
Female sex, n (%)	132 (41.9)	32 (47.1)	100 (40.5)
Admission ward: medical, n (%)	148 (47.0)	32 (47.1)	116 (47.0)
Admission ward: surgical, n (%)	82 (26.0)	12 (17.6)	70 (28.3)
Admission ward: ICU, n (%)	85 (27.0)	24 (35.3)	61 (24.7)
Baseline eGFR, mean (SD), mL/min/1.73m²	72.4 (28.4)	48.2 (24.6)	79.0 (26.2)
Baseline eGFR <60, n (%)	98 (31.1)	42 (61.8)	56 (22.7)
Baseline eGFR <30, n (%)	22 (7.0)	16 (23.5)	6 (2.4)
Hypertension, n (%)	178 (56.5)	48 (70.6)	130 (52.6)
Diabetes mellitus, n (%)	112 (35.6)	32 (47.1)	80 (32.4)
Chronic kidney disease known, n (%)	78 (24.8)	32 (47.1)	46 (18.6)
Cirrhosis, n (%)	18 (5.7)	12 (17.6)	6 (2.4)
Sepsis at exposure initiation, n (%)	112 (35.6)	42 (61.8)	70 (28.3)
Hypotension during exposure, n (%)	78 (24.8)	38 (55.9)	40 (16.2)
Concurrent loop diuretics, n (%)	118 (37.5)	42 (61.8)	76 (30.8)
Concurrent ACEi/ARB, n (%)	98 (31.1)	28 (41.2)	70 (28.3)
Contrast within 7 days, n (%)	62 (19.7)	26 (38.2)	36 (14.6)
Two or more nephrotoxic exposures, n (%)	148 (47.0)	52 (76.5)	96 (38.9)

3.2 AKI Incidence by Exposure Category

AKI by KDIGO criteria occurred in 68 of 315 patients (21.6%). Incidence varied substantially by antibiotic exposure category (Figure 1), with the highest rates seen in colistin and polymyxin B exposures (38.5%), amphotericin B (33.3%), and the vancomycin-plus-piperacillin-tazobactam combination (27.8%). Vancomycin alone, despite being the most frequently prescribed agent, showed comparatively modest AKI rates of 14.3% well below the rate in combination with piperacillin-tazobactam. Piperacillin-tazobactam given alone, in contrast, was associated with the lowest AKI rate (11.4%), supporting the hypothesis that the combination represents more than simple additivity.

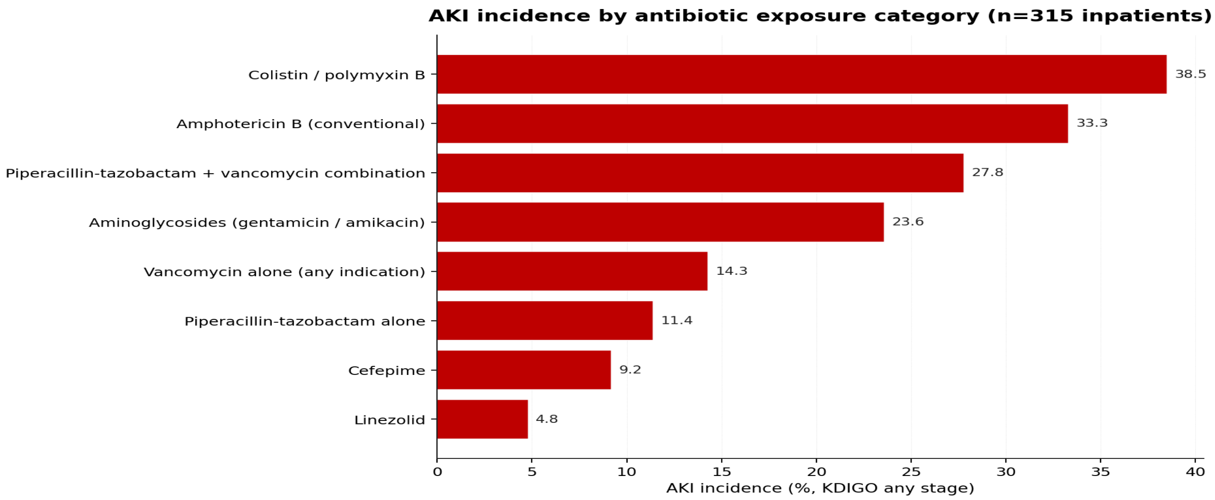

Figure 1. AKI incidence by antibiotic exposure category. Rates represent any-stage KDIGO AKI during exposure or within 14 days of completion.

Table 2. AKI severity by antibiotic exposure category.

Exposure category	n exposed	Any AKI, n (%)	Stage 2-3, n (%)	Required RRT, n (%)
Vancomycin alone	168	24 (14.3)	6 (3.6)	2 (1.2)
Piperacillin-tazobactam alone	88	10 (11.4)	2 (2.3)	0 (0.0)
Vanc + Pip-tazo combination	108	30 (27.8)	12 (11.1)	4 (3.7)
Aminoglycosides	72	17 (23.6)	8 (11.1)	2 (2.8)
Colistin / polymyxin B	26	10 (38.5)	6 (23.1)	2 (7.7)
Amphotericin B	18	6 (33.3)	4 (22.2)	1 (5.6)
Cefepime	98	9 (9.2)	2 (2.0)	0 (0.0)
Linezolid	62	3 (4.8)	0 (0.0)	0 (0.0)
Two or more nephrotoxic agents	148	52 (35.1)	20 (13.5)	6 (4.1)

3.3 Interaction with Baseline Renal Function

The AKI risk gradient across baseline eGFR strata was steep (Figure 2). Patients with eGFR ≥90 at baseline showed single-digit AKI rates for most antibiotic classes, while those with eGFR <30 reached rates above 40% for combination exposures and above 50% for colistin and amphotericin B. The interaction is operationally important: structured renal-aware prescribing could focus most intensively on the high-risk cells of this matrix, where incidence approaches or exceeds 30-40%.

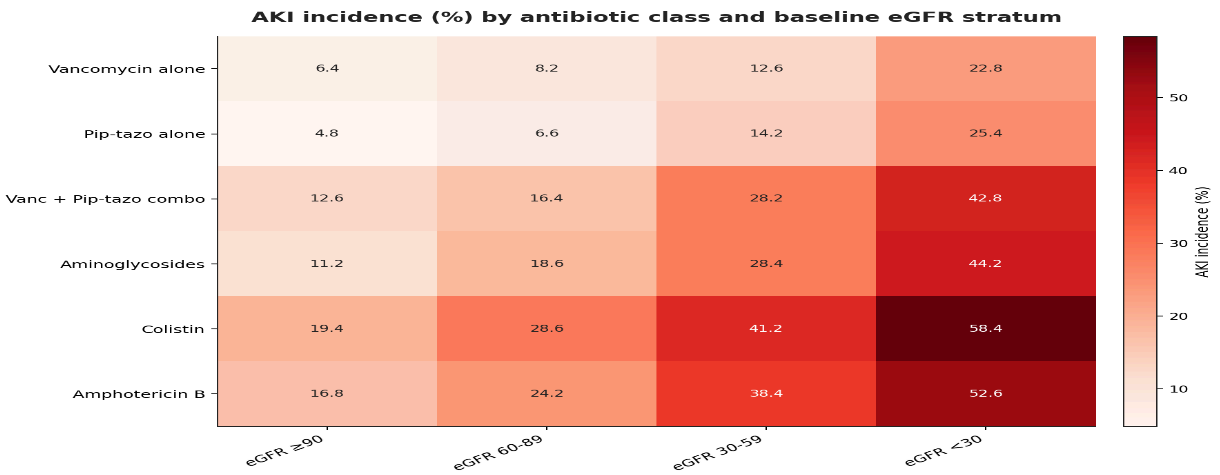

Figure 2. AKI incidence (%) by antibiotic class and baseline eGFR stratum. Darker shading indicates higher incidence.

3.4 Multivariable Risk Analysis

Multivariable Cox regression identified ten independent predictors of antibiotic-associated AKI (Figure 3). Severe baseline renal impairment (eGFR <30) carried the strongest single association (HR 7.85). Among modifiable factors, hypotension during exposure (HR 3.84), multiple concurrent nephrotoxic exposures (HR 3.18), and concurrent contrast administration (HR 2.42) were the most amenable to intervention. The presence of cirrhosis with ascites independently increased risk, reflecting the combined effects of hypoalbuminaemia, altered tissue distribution, and frequent diuretic exposure in this population.

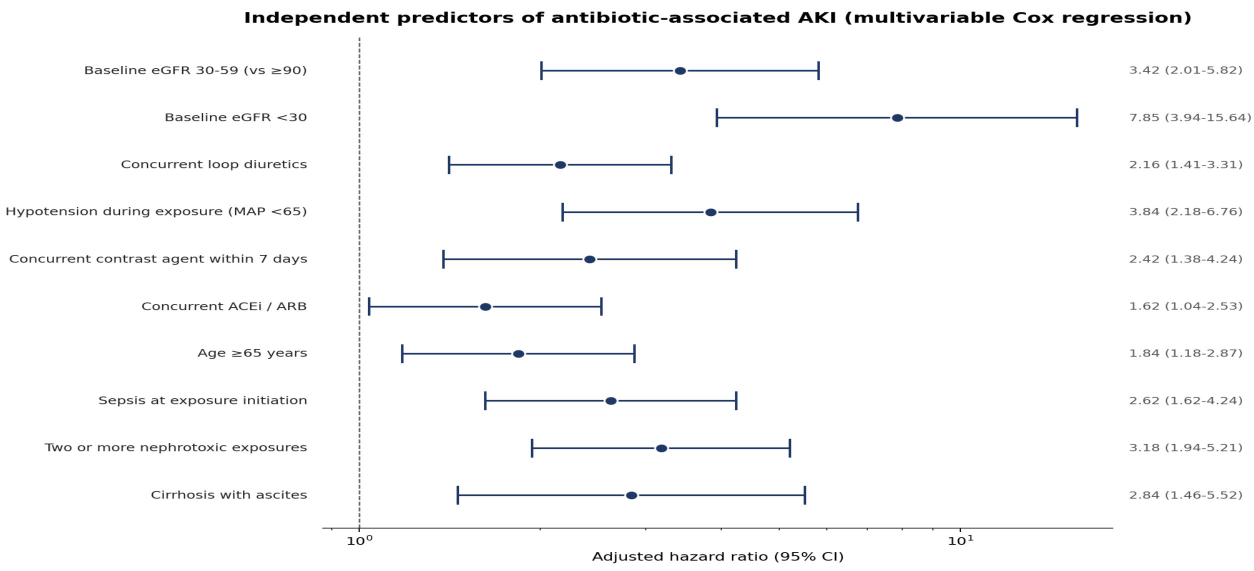

Figure 3. Independent predictors of antibiotic-associated AKI from multivariable Cox regression.

3.5 Recovery and Outcomes

Creatinine recovery trajectories differed substantially by AKI stage (Figure 4). Stage 1 AKI typically peaked around day 5-7 and recovered toward baseline within 14-30 days. Stage 2 AKI showed a higher peak and slower recovery, with most patients reaching near-baseline values by day 60. Stage 3 AKI showed the highest peak and incomplete recovery in the majority of cases, with mean creatinine values at day 60 remaining nearly double baseline. Among the 8 stage 3 cases, 3 required dialysis during admission; 1 remained dialysis-dependent at 60 days.

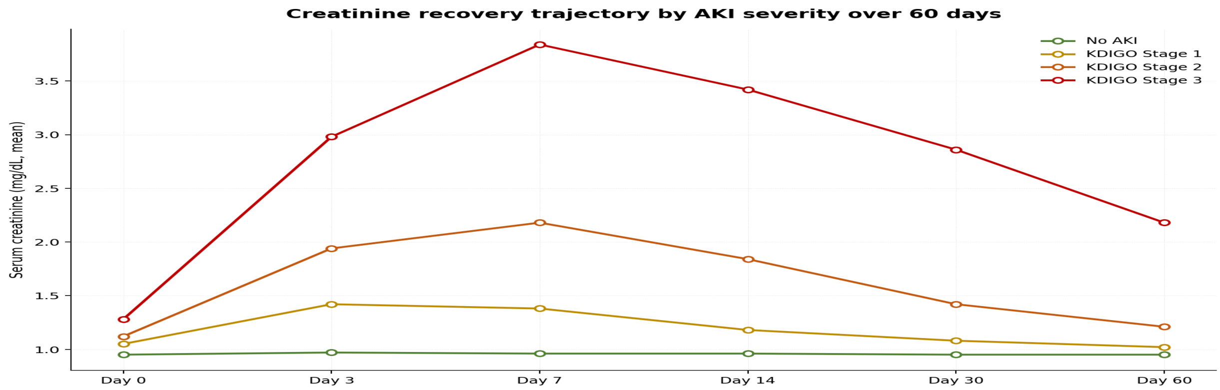

Figure 4. Creatinine recovery trajectory by AKI severity over 60 days. Stage 3 AKI showed incomplete recovery in most cases.

Table 3. Recovery patterns and outcomes by AKI status.

Outcome	No AKI (n=247)	Stage 1 (n=41)	Stage 2 (n=19)	Stage 3 (n=8)
Complete recovery at day 30, n (%)	-	36 (87.8)	12 (63.2)	2 (25.0)
Complete recovery at day 60, n (%)	-	38 (92.7)	13 (68.4)	3 (37.5)
Persistent renal impairment at 60 days, n (%)	-	3 (7.3)	6 (31.6)	5 (62.5)
Requires RRT during admission, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	3 (37.5)
RRT-dependent at 60 days, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)
Length of stay, median (IQR), days	9 (6-14)	14 (10-19)	19 (14-28)	26 (18-42)
In-hospital mortality, n (%)	18 (7.3)	6 (14.6)	6 (31.6)	4 (50.0)
30-day mortality, n (%)	22 (8.9)	8 (19.5)	8 (42.1)	5 (62.5)
Discharge with stage-down antibiotic, n (%)	148 (59.9)	18 (43.9)	6 (31.6)	2 (25.0)

3.6 Stewardship Opportunity Gaps

Table 4. Documented stewardship gaps in the AKI cohort.

Stewardship element	Cases with AKI (n=68)	Cases without (n=247)
Baseline creatinine documented within 48h pre-exposure	58 (85.3)	234 (94.7)
Renal-adjusted dose used where indicated	32/52 (61.5)	148/194 (76.3)
Therapeutic drug monitoring performed for relevant agents	42/56 (75.0)	158/188 (84.0)
Trough levels within target range	18/42 (42.9)	118/158 (74.7)
De-escalation review at 48-72h	26 (38.2)	132 (53.4)
Avoidance of preventable duplication	48 (70.6)	218 (88.3)
Pharmacy alert acted on	52/62 (83.9)	178/192 (92.7)
Daily creatinine surveillance during exposure	56 (82.4)	202 (81.8)
Documented hydration strategy in high-risk patients	18/38 (47.4)	78/108 (72.2)

IV. Discussion

Across 315 hospitalised adults receiving antibiotics with documented nephrotoxic potential, AKI occurred in approximately one in five, with a steep risk gradient across antibiotic class, baseline renal function, and concurrent exposures. Three observations from this cohort have practical implications for inpatient prescribing. First, the magnitude of the vancomycin-plus-piperacillin-tazobactam interaction stands out. Either agent alone produced AKI rates broadly consistent with the lower end of the published literature (14% and 11% respectively). The combination produced a rate of 28% roughly the sum of the two, which is itself inconsistent with simple additive risk. The mechanism remains debated, with proposed contributions from acute interstitial nephritis, altered renal blood flow, and pseudo-creatinine elevation from cefepime cross-reactivity. Regardless of mechanism, the operational implication is clear: alternative empirical combinations covering similar pathogen spectra, such as vancomycin with cefepime or with meropenem, should be preferred in patients at elevated baseline AKI risk (Jha, Kumar,, & Neha, 2026; Bhatnagar, Kumar,, & Shivam, 2026). Second, the modifiable risk factors hypotension, multiple nephrotoxic exposures, concurrent contrast together carry the bulk of the preventable AKI burden. Hypotension during exposure quadrupled risk; more aggressive haemodynamic management in patients receiving nephrotoxic antibiotics, including consideration of vasopressor support to maintain mean arterial pressure during sepsis episodes, has a clearly demonstrable case. Contrast administration within 7 days of nephrotoxic antibiotic exposure should be reviewed for necessity, with deferral or alternative imaging considered where feasible (Jha, Kumar,, & Neha, 2026; Agarwal, Kumar,, & S, 2026; Bhatnagar, Kumar,, & Shivam, 2026). Third, the stewardship gap documented in Table 4 is substantial. Approximately 40% of patients who later developed AKI had not undergone documented de-escalation review at 48-72 hours, and over half of those with relevant drug-level monitoring had at least one trough value outside the target range. These are not failures of knowledge they are failures of operational implementation under workload pressure. AI-supported decision support integrated into the prescribing workflow has shown promise in similar contexts and warrants broader deployment (Deepa et al., 2026; Devi et al., 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025; Vinodh, Subramani,, & Vettriselvan, 2026; Subramani, Chillagattu, et al., 2026; Selvi et al., 2026). Implementation considerations include pharmacy-led nephrotoxin review at admission for high-risk patients, automated dose-adjustment prompts based on real-time eGFR, structured de-escalation review embedded in routine rounds, and audit-and-feedback cycles for prescribing practice. Patient education about hydration during outpatient antibiotic courses is a less discussed but worthwhile complement (Catherine, Gupta, Gopi,, & Swadhi, 2025; Vettriselvan, Ramya, et al., 2026). For intensive care units specifically, hypotension surveillance during nephrotoxic exposures should be tightened with explicit triggers for haemodynamic optimisation (Kumar, Kumar,, & Dhabhai, 2026; Ahluwalia, Gupta,, & Chaudhary, 2026). Limitations include the single-centre observational design, the imperfect ascertainment of alternative AKI aetiologies (sepsis, hypovolaemia, obstruction may have contributed beyond what adjudication could exclude), the modest sample sizes for colistin and amphotericin B which limit precision for those classes, and the 60-day follow-up which does not capture longer-term progression to chronic kidney disease in patients with partial recovery. The cohort was identified through pharmacy exposure rather than randomised allocation, so apparent class effects incorporate clinical-selection bias for the underlying indication.

V. Conclusion

Antibiotic-associated AKI affected approximately one in five hospitalised adults receiving nephrotoxic-potential agents in this prospective pharmacovigilance cohort. The risk gradient across antibiotic class, baseline renal function, and concurrent exposures was steep, with the vancomycin-piperacillin-tazobactam combination, severe baseline renal impairment, hypotension during exposure, and multiple concurrent nephrotoxin exposure as the dominant determinants. Structured renal-aware stewardship integrating dose-adjustment algorithms, hypotension surveillance, contrast review, and structured de-escalation offers a practical pathway to substantial preventable AKI reduction.

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