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Incidence of Acute Kidney Injury among Adult Hospitalized Patients with Carbapenem Resistant Gram-Negative Infections Who Received Early Targeted Treatment with a Newer β-Lactam-, Colistin, or Aminoglycoside-Containing Regimen

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BACKGROUND

- Data indicates that hospitalized patients, regardless of cause, who developed even modest cases of acute kidney injury (AKI) are at increased risk of short-term unfavorable outcomes, including death (PMID: 16177006).
- While the deleterious consequences of AKI are well-described across most therapeutic domains, there are scant data on incidence and associated outcomes of AKI among hospitalized adult patients with carbapenem resistant gram-negative infections (CR-GNIs).
- This study sought to characterize the incidence of AKI and associated outcomes among hospitalized adult patients with CR-GNIs who received early directed treatment with a newer β-lactam (BL), polymyxin (PB), or aminoglycoside (AG)-containing regimen.

OBJECTIVES

- Determine the incidence of AKI among adult, non-dialysis dependent, hospitalized patients with CR-GNIs, overall and by treatment received (BL, PB, or AG).
- Delineate the outcomes associated with the development of AKI among adult, non-dialysis dependent, hospitalized patients with CR-GNIs, overall and by treatment received (BL, PB, or AG).

METHODS

Study Design and Population

- Retrospective, multi-centered observational study of hospitalized adult patients in the PINC AI Healthcare Database

Study Criteria

- Age ≥ 18 years old
- Inpatient hospitalization discharged between 2016 to 2020
- Identification of a CR-GN pathogen on a clinical culture that is consistent with pneumonia (PNA), bloodstream infection (BSIs), or complicated urinary tract infection (cUTIs)
- For PNA and cUTIs, evidence of a clinical diagnosis defined by algorithms based on ICD-10 diagnosis or procedure codes.
- Receipt of a newer BL, PB, or AG within 3 days of index CR-GN culture collection day
- Treatment with BL, PB, or AG for ≥3 consecutive days (first received for ≥3 day defined treatment group)
- No receipt of any renal replacement therapy prior to index treatment Serum creatinine ≤2 mg/dL ± 2 d of index treatment initiation day
- Serum creatinine value data ≥ 2 days after index treatment day

METHODS CONTD.

Baseline Covariates

- Demographics
  - Age, sex, race, and ethnicity
- Clinical Characteristics
  - Charlson Comorbidity Index, hospital length of stay (LOS) prior to index CR-GN culture collection day, residence in ICU on index CR-GN culture collection day, infection type, CR-GN pathogen on index culture, receipt of nephrotoxic medication between admission to index CR-CN culture collection day, and S_{CR} on index treatment day

Comparison Treatment Groups

- **Newer BL:** Ceftolozane/Tazobactam, Ceftazidime/Avibactam, Imipenem/Relebactam, Cefiderocol, and Meropenem/Vaborbactam
- **PB:** Colistin
- **AG:** Gentamicin, Tobramycin, and Amikacin

Outcomes

- On-Treatment AKI was based on RIFLE criteria: 50% increase in targeted treatment day 1 $S_{CR,}$ assessed from index treatment day through 3 days after BL, PB, or AG discontinuation
- In-Hospital Mortality
- Hospital LOS Post-Index CR-GN culture collection day

Statistical Methods

- Bivariate analyses
  - Chi-square tests was used to compare categorical baseline covariates and outcome variables between treatment groups and outcomes and presence of AKI.
  - Analysis of variance and Kruskal-Wallis test were used to compare ordinal/continuous baseline covariate variables between treatment groups.
- Multivariable analyses
  - Logistic regression was used to evaluate the association between AKI and treatment and in-hospital mortality and AKI.
  - Generalized linear modeling was used to evaluate the association between hospital LOS and AKI.

RESULTS

Study Population Characteristics

- 1,061 patients met study inclusion criteria across 157 hospitals
  - 33.8% of hospitals were Teaching Hospitals
  - 61.8% of hospitals were from the Southern US Census Region
- The majority received BL (45%), followed by AG (36%), and PB (19%)

Table 1. Baseline Characteristics of Treatment Groups

	Newer Beta-Lactam (n=475)	Aminoglycoside (n=387)	Polymyxins (n=199)
Mean age, years (SD)	63.2 (15.3)	60.0 (16.7)	59.3 (16.8)
Gender: male	67%	66%	65%
Median [IQR] Charlson Comorbidity Index	3 [2,5]	2 [1,4]	3 [2,4]
CR-GN on index culture (most common)			
Acinetobacter baumannii	3%	5%	34%
Escherichia coli	3%	3%	2%
Klebsiella pneumoniae	21%	7%	26%
P. aeruginosa	66%	68%	38%
S. maltophilia	3%	10%	23%
Infection type			
Pneumonia	58%	71%	84%
Complicated UTI	43%	33%	20%
Bloodstream infection	23%	12%	17%
Median [IQR] LOS prior to index CR-GN culture, measured in days	1 [1,5]	2 [1, 6]	2 [1, 6]
Residence in ICU at index CR-GN culture	39%	42%	53%
Receipt of concomitant nephrotoxic medications	36%	40%	48%
Median [IQR] Scr on index treatment day, measured in mg/dL	0.76 [0.50, 1.15]	0.67 [0.49, 0.90]	0.69 [0.46, 1.00]

Figure 1. Bivariate Association Between Treatment and Outcomes

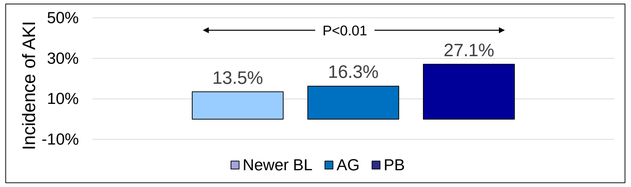
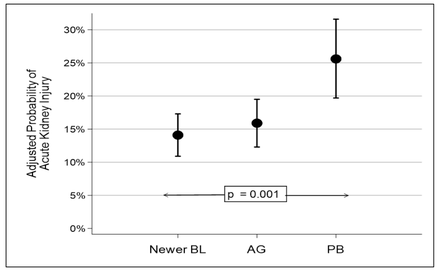
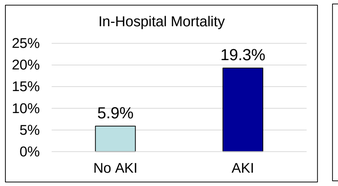


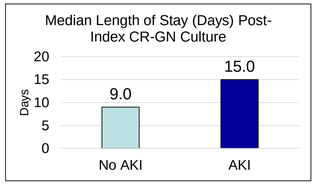
Figure 2. The Adjusted Probability of AKI among Patients Who Received a Newer BL, PB-, or AG-Containing Regimen



The logistic regression model adjusted for treatment group, time from admission to index culture, initial serum creatinine, age, gender, race, Charlson comorbidity index, ICU admission on or before index culture, emergency admission status, and infection type (cUTI, blood, respiratory)

Figure 3. Associations Between Presence of AKI and Outcomes





CONCLUSIONS

- Incidence of AKI among hospitalized patients with serious CR-GNIs was highest in pts who received an early-targeted polymyxin-containing regimen.
- Occurrence of AKI was associated with increased in-hospital mortality and longer post-index culture hospital LOS.

https://bit.ly/3QINrHC

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