# Incidence and Risk Factors for AKI in Preterm Infants Treated with Vancomycin

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## Abstract

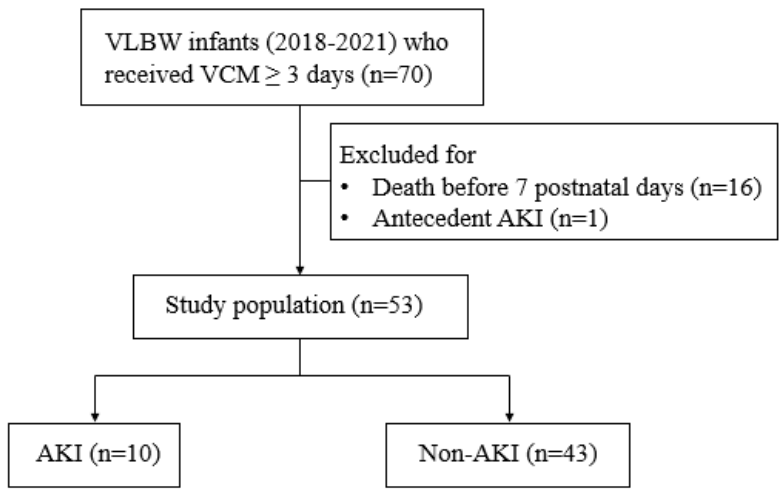
We analyzed electrical medical record of 320 pediatric patients with venous pH below 7.25 who visited a pediatric emergency room (PER) of a tertiary hospital in South Korea. We found a high incidence of acute kidney injury (AKI) among acidotic patients, and those with metabolic acidosis and especially high anion gap metabolic acidosis were at a higher risk of AKI.

## Introduction

- Vancomycin (VCM) is one of the known causes of AKI, which can be life-threatening in preterm infants.
- Perinatal characteristics, such as gestational age or birthweight, and neonatal morbidities, including patent ductus arteriosus or necrotizing enterocolitis (NEC), may contribute to VCM-induced AKI.
- Recent studies have suggested that piperacillin-tazobactam (TZP) may aggravate VCM-induced nephrotoxicity in adults and adolescents.
- This study explored the factors, including the concomitant use of TZP, associated with VCM-induced AKI in preterm infants.

## Methods and Materials

- Retrospective single-center study
  - Preterm infants with birth weight < 1,500g
  - Who were born between 2018 and 2021 in a tertiary center
  - Who received VCM for a minimum of 3 days
- AKI defined as a minimum increase in serum creatinine (sCr) of 0.3 mg/dL, and an increase in sCr of at least 1.5 times the baseline level during VCM use and up to 1 week following VCM discontinuation




## Patient Characteristics (n=53)

| | AKI (n=10) | AKI (n=43) | P value |
|---|---|---|---|
| Gestational age, week | 24.0 [24.0-25.0] | 26.0 [24.0-28.0] | 0.068 |
| Birth weight, g | 675 [670-866] | 770 [600-955] | 0.802 |
| Oligohydramnios | 1 (14.3) | 6 (15.0) | 1.000 |
| Male | 7 (70.0) | 16 (57.1) | 0.552 |
| IUGR | 7 (10.0) | 10 (23.3) | 0.618 |
| Apgar score, 1 min | 3.0 ± 1.6 | 3.6 ± 2.0 | 0.412 |
| Apgar score, 5 min | 6.0 ± 1.9 | 6.3 ± 2.3 | 0.745 |

## Results

1. AKI occurred in 10 (18.9%) at 7 days (3 to 11 days) after starting VCM.
2. Gestational age at birth, birth weight, pathogen-proven sepsis, duration of VCM, postmenstrual age at starting VCM, highest concentration of VCM, patent ductus arteriosus at starting VCM, and co-administration of TZP were not statistically different between the AKI & the non-AKI groups.
3. A history of NEC was significantly high in the AKI group (5 (50.0%) vs 2 (4.7%), OR 20.05 [3.11-134.94], p-value 0.002).
4. In multivariable logistic regression, gestational age at birth was significantly differed between the AKI & the non-AKI group.
5. Backward stepwise regression showed that AKI was associated with low gestational age (adjusted OR: 0.58, 95% CI: 0.35–0.98) and a history of NEC (37.65, 3.08–459.96).

## Neonatal morbidity and vancomycin related factors

| | AKI (n=10) | AKI (n=43) | Univariate OR (95% CI) | P |
|---|---|---|---|---|
| Sepsis (pathogen (+)) | 5 (50.0) | 16 (37.2) | 1.69 (0.42-6.74) | |
| Duration of VCM (d) | 5.0 [3.0–9.0] | 4.0 [2.0-9.0] | 1.02 (0.94–1.10) | 0.701 |
| PMA at VCM, week | 27.8 [25.1–40.4] | 33.0 [29.2–38.7] | 0.96 (0.87–1.05) | 0.356 |
| Highest conc. of VCM (μg/mL) | 38.5 [29.8–60.5] | 36.2 [25.1–44.1] | 1.04 (0.99–1.10) | 0.088 |
| PDA at starting VCM | 7 (70.0) | 18 (41.9) | 3.24 (0.74–14.26) | 0.12 |
| Co-Mx of TZP | 4 (40.0) | 21 (48.8) | 0.70 (0.17-2.83) | 0.615 |
| NEC | 5 (50.0) | 2 (4.7) | 20.05 (3.11–135) | 0.002 |

*VCM, vancomycin; PMA, postmenstrual age; PDA, patent ductus arteriosus; TZP, piperacillin-tazobactam, NEC, necrotizing enterocolitis; AKI, acute kidney injury; OR, odds ratio; CI, confidence interval.*

## Multivariable analyses for AKI

| | AKI (n=10) | AKI (n=43) | §Multivariate OR (95% CI) | P |
|---|---|---|---|---|
| Gestational age, week | 24.6 [24.3–25.6] | 26.4 [24.4-28.4] | 0.58 (0.35–0.98) | 0.042 |
| PDA at starting VCM | 7 (70.0) | 18 (41.9) | 5.23 (0.67–41.05) | 0.115 |
| NEC | 5 (50.0) | 2 (4.7) | 37.65 (3.08–459.96) | 0.005 |

*Data are presented as median [interquartile range], or n (%). PDA, patent ductus arteriosus; NEC, necrotizing enterocolitis; AKI, acute kidney injury. §Adjusted for gestational age and PDA at initiation of VCM and NEC.*

## Conclusions

In very-low birthweight infants, a lower gestational age and history ofnecrotizing enterocolitis, but not concomitant use of piperacillin-tazobactam, wereassociated with VCM-induced AKI.