Urinary NGAL are Elevated in Neonates who Develop AKI after General Surgical Procedures

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Background

- Acute Kidney Injury (AKI) commonly occurs in critically ill neonates after surgery [1-4]
- AKI diagnosis by serum creatinine and urine output has significant limitations in this population [1]
- Urinary neutrophil gelatinase-associated lipocalin (uNGAL) has been shown to predict AKI in pediatric and neonatal cohorts [5-6]
- The association of uNGAL with AKI in neonates after general surgical intervention is unknown

Methods

- Prospective observational study
- Neonates undergoing a general surgical procedure, excluding a laparoscopic gastrostomy tube placement
- AKI was classified by 2014 modified Neonatal KDIGO Classification criteria (*Table 1*)
- Urine was obtained pre-operatively and at 12, 24, 36, 48, 72 and 96 hours post-operatively
- uNGAL was measured by The NGAL Test™ (BioPorto, Denmark)
- Statistical methods include chi-square, t-test, Mann Whitney U

Table 1. 2014 Modified Neonatal KDIGO Classification of AKI

Stage	Serum Creatinine Definition	Urine Output Definition
0	No change in SCr or rise <0.3 mg/dL	≥ 0.5 mL/kg/h
1	SCr rise ≥ 0.3 mg/dL in 48 h or SCr rise ≥1.5–1.9 × reference SCr within 7 d	<0.5 mL/kg/h for 6 to 12 h
2	SCr rise ≥2.0–2.9 × reference SCr	<0.5 mL/kg/h for ≥ 12 h
3	SCr rise ≥3 × reference SCr or SCr ≥2.5 mg/dL or Receipt of dialysis	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h

Results

- 88 neonates had 113 surgical procedures
- At the time of surgical intervention, average corrected GA was 40 ± 7 weeks
- 37 (33%) occurrences of AKI post-operatively.
- Average time of AKI diagnosis by serum creatinine and urine output was 24-48 hours post-operatively
- Pre-operative NGAL was not associated with development of AKI (55 ng/mL vs. 34 ng/mL, p=0.24)
- Following surgical intervention, uNGAL values were higher in infants with neonatal AKI vs. no AKI at all measured time points (*Figure 1, Table 2)*
- uNGAL rises as early as 12 hours post-operative with the greatest statistical significance found at 24 hours post-op, preceding AKI diagnosis by standard definitions. (*Table 2)*
- 17/37 (46%) occurrences were classified as severe AKI (stage 2 or stage 3) with 5 patients meeting the definition for both serum creatinine and urine output (*Table 3)*
- Peak post-operative uNGAL was associated with the development of post-operative AKI (417ng/mL vs. 102 ng/mL, p value <0.0001)

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Results

Table 2. Median [IQR] uNGAL levels in patients with vs. without AKI after surgery

	Pre-op uNGAL	12 hr uNGAL	24 hr uNGAL	36 hr uNGAL	48 hr uNGAL	72 hr uNGAL	96 hr uNGAL
All	(n=74)	(n=105)	(n=103)	(n=88)	(n=65)	(n=97)	(n=86)
No AKI (n=76)	34 [14-103]	29 [12-102]	38 [14-129]	34 [17-101]	37 [14-148]	38 [16-96]	41 [10-111]
AKI (n=37)	55 [11-315]	206 [27-1280]	199 [66-384]	190 [38-573]	131 [42-463]	211 [34-770]	65 [24-371]
p value	0.24	0.0033	<0.0001	0.0009	0.0008	0.0039	0.0218

Figure 1. Median uNGAL levels in patients with vs. without AKI

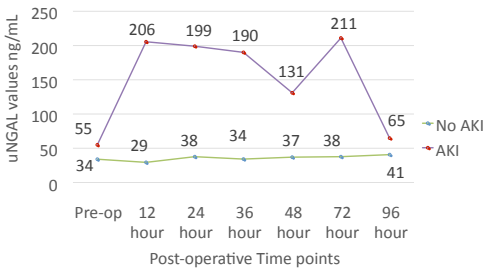

Table 3. Stage and diagnosis for patients with AKI

Stage	All	Serum Creatinine (n=11)	Urine Output (n=30)
1	23	8	15
2	7	2	5
3	11	1	10

**5 patients met criteria for both serum creatinine and urine output*

Conclusions

- Post-operative urine NGAL is elevated in infants who develop AKI
- While peak NGAL levels occurred at 24 hours post-operatively statistically significant elevations occur as early as 12 hours post-operative, which preceded serum creatinine based AKI
- We suggest that uNGAL could be used as an earlier biomarker for detection of renal insult and allow for earlier modifications to treatment plans and avoidance of nephrotoxic medication exposure

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