An Exploration of the Association of Sex and Pubertal Status with AKI and AD in Critically Ill Children

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Background and Purpose

- Animal studies have shown that estrogen is protective in ischemic AKI and testosterone is associated with worse outcomes
- Recent epidemiologic studies suggest that males have higher rates of hospital-acquired AKI, but females have worse kidney outcomes after AKI
- Few investigators have explored the effects of sex on pediatric AKI or AKD
- We questioned if pubertal status impacts the association of sex and AKI or AKD in children
- Objective: Examine the association of sex and pubertal status with AKI and AKD in a general pediatric ICU cohort

Methods

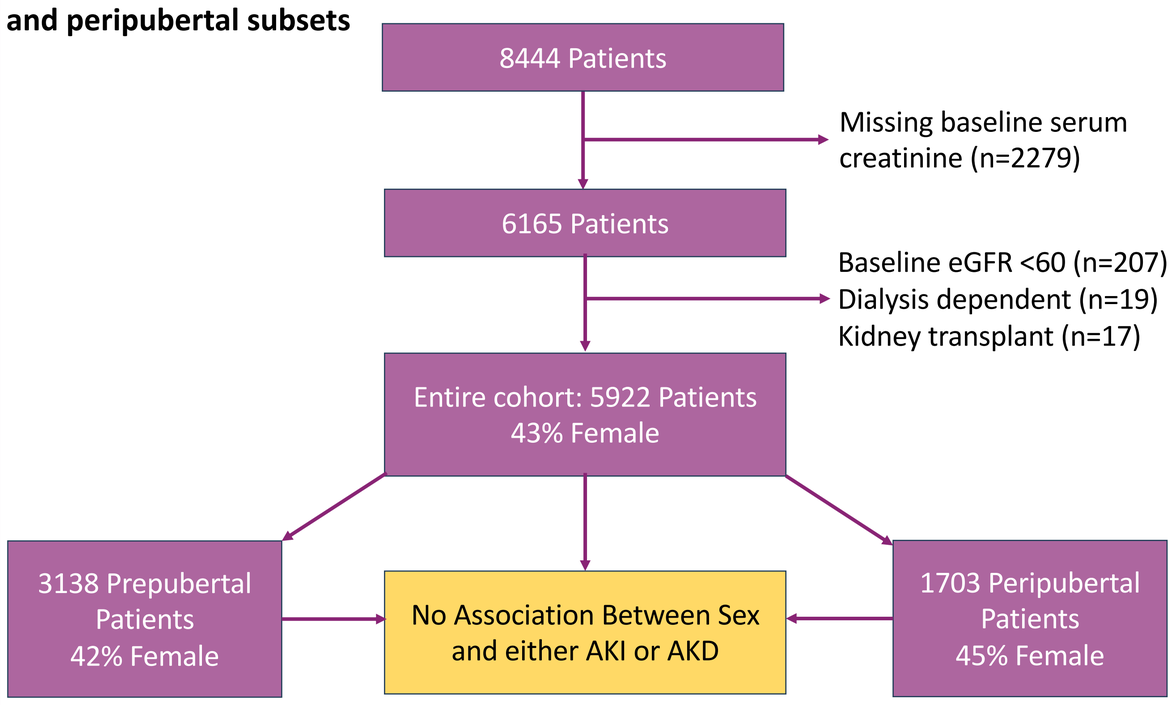
- Retrospective cohort study of all patients 60 days-18 years of age admitted the UPMC Children's Hospital of Pittsburgh PICU between 2009-2016
- Excluded patients who at the time of admission:
  - Were dialysis dependent
  - Did not have a baseline serum creatinine available
  - Had a baseline eGFR <60 ml/min/1.73m2
  - Had a kidney transplant
- The primary outcome of the study is the development of AKI or AKD through 30 days, defined by KDIGO
- Significant variables from univariable analyses are included for a final multivariable regression model
  - Severity of illness assessed using the Pediatric Index of Mortality (PIM) 2 score
- Patients were stratified by puberty status based on age

Table 1. Age designations for pubertal status

Pubertal Status	Age (Years)
Prepubertal	≤ 8 years
Peripubertal	9-15
Postpubertal	≥ 16

Results

Figure 1. Consort diagram and results for the entire cohort and the prepubertal and peripubertal subsets



Results (continued)

- In the overall cohort of critically ill children, sex was not significantly associated with the development of AKI or AKD
- Also in the prepubertal and peripubertal subgroups, there was no significant association between sex and either AKI or AKD
- However, in the postpubertal subset of patients, sex, BMI, baseline creatinine, and severity of illness were significantly associated with AKI and AKD in univariable analyses

Table 2. Multivariable logistic regression of risk factors for AKI and AKD in postpubertal critically ill children

Outcome: AKI n=300 (28%)	Odds Ratio	95% CI	p-value
Sex (female)	0.61	0.44-0.82	**<0.01**
BMI (kg/m^2)	1.05	1.03-1.08	**<0.01**
Baseline Creatinine (mg/dL)	0.61	0.28-1.33	0.21
PIM-2 Score	5.92	0.93-37.95	0.06
Outcome: AKD n=149 (14%)			
Sex (female)	0.60	0.40-0.91	**0.01**
BMI (kg/m^2)	1.03	1.00-1.06	**0.02**
Baseline Creatinine (mg/dL)	4.54	1.58-13.08	**<0.01**
PIM-2 Score	3.96	0.46-33.73	0.21

- Female sex was independently associated with decreased incidence of AKI and AKD in postpubertal patients

Conclusions

- In a broad cohort of critically ill children, female sex is protective against hospital-acquired AKI and AKD at 30 days in postpubertal patients
- There was no association of sex with hospital-acquired AKI and AKD in prepubertal or peripubertal patients
- Future studies could include novel biomarkers of kidney dysfunction
- Implications of our results include:
  - Future pediatric studies investigating sex as a biological variable should consider pubertal status
  - Further work is needed for exploring sex as biological variable in differing AKI phenotypes
  - Studies similar to ours could investigate the role of sex in longer term kidney outcomes like CKD and ESKD