Trauma of Origin - The Impact of Maternal Acute Kidney Injury on Progeny Growth
AKI & CRRT Conference

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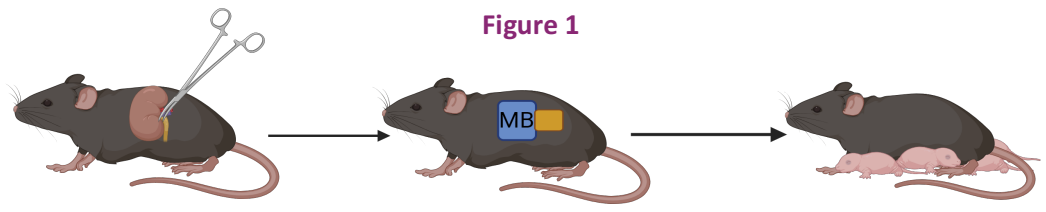
Abstract

Acute Kidney Injury (AKI) results in both short- and long-term systemic sequelae. The impact of AKI on future generations, remains unclear. Our study focuses on the long-term impact that AKI in young, healthy, female mice has on their progeny, with a focus on growth outcomes and baseline kidney health.

Methods

- Healthy, wild-type BLK/6J female mice either underwent bilateral ischemia reperfusion AKI (25 minutes), surgical sham procedure, or were unmanipulated.
- Serum BUN was measured 24hrs post-procedure (AKI vs Sham).
- Animals recovered for 2 weeks then underwent transcutaneous glomerular filtration (tGFR) measurement to assess kidney function.
- Females (referred to as Dams) were bred with wild-type C57BLK/6J males and allowed to deliver naturally. **Figure 1**
- Serial testing of weight and length of progeny occurred weekly, starting at birth through 42 days of age.
- Progeny underwent additional testing including tGFR, body composition analysis, BUN and serum creatinine, and cross-sectional glomerular count via Jacalin stain. **Figure 2**

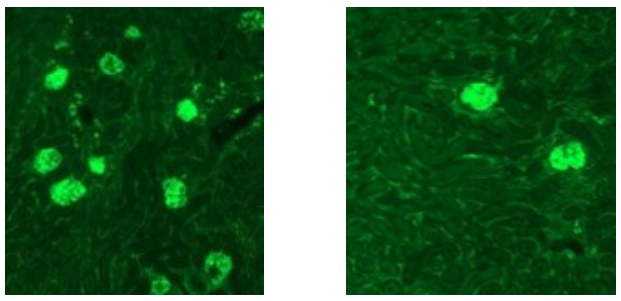
Figure 1

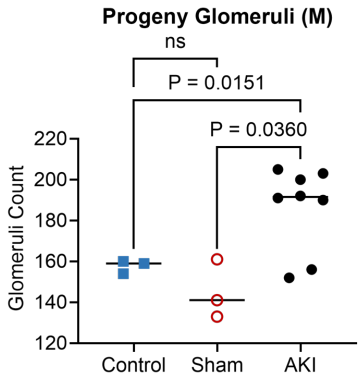


Results

- AKI dams with an elevated 24hr post-procedure BUN bore smaller litters.
- Male progeny from AKI-dams had lower birth weights than sham or control male progeny (p=0.02). There was no significant difference in birth weights amongst the female progeny cohorts.
- By day 7, AKI-progeny weights "caught up" to their counterparts.
- After day 35, male progeny from AKI-dams surpassed sham and control males (p=0.04). **Figure 3**
- Male and female progeny from AKI-dams were shorter than sham or control counterparts (p=0.005 for males and p=0.01 for females). **Figure 4**
- By day 7 both male and female lengths "caught up" to their counterparts.
- At day 42 males and females from AKI-dams had surpassed the lengths of their counterparts (p=0.0002 in males and p=0.04 in females). **Figure 5**
- Glomerular count in males from AKI-dams were found to be higher than other progeny, male or female (p=0.01). **Figure 2**

Figure 2





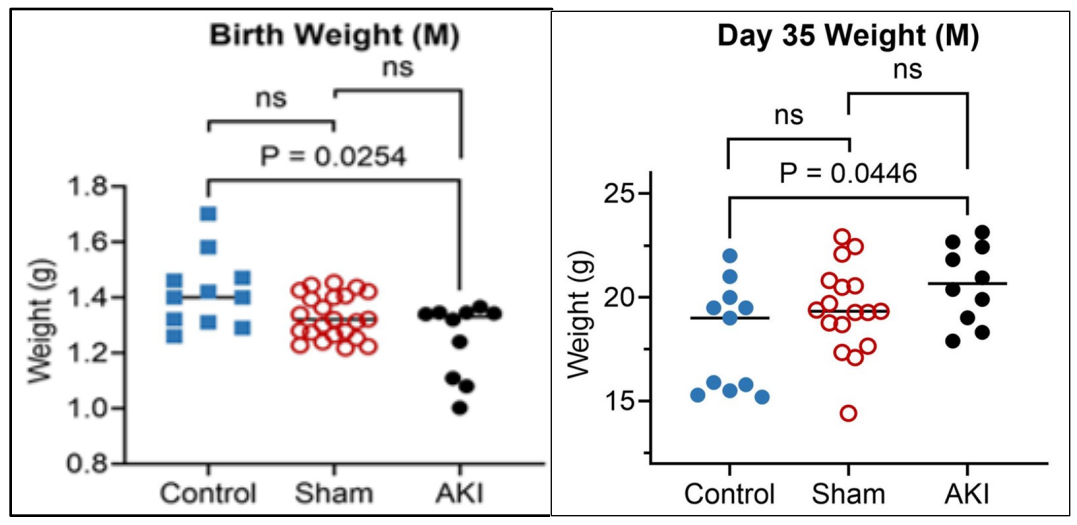


Figure 3

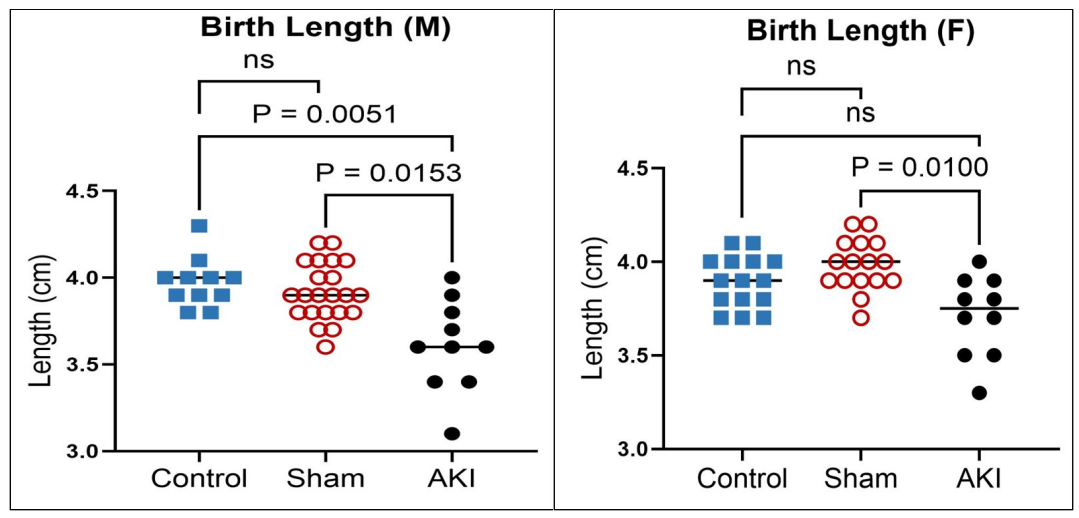


Figure 4

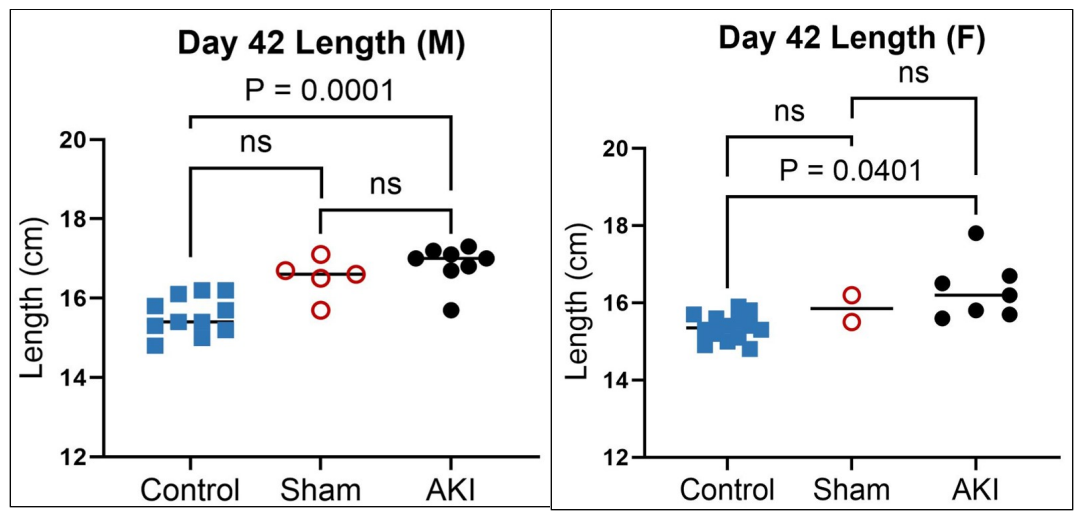


Figure 5

Conclusions

Based on the findings of this study AKI in healthy females impacts litter size as well as the birth weight and lengths of progeny. Sex is an important biological variable in progeny outcomes, with males being more effected than females. The progeny had the most noticeable differences in weight and length at birth, however their growth caught back up to the progeny of the sham and unmanipulated control dams. Further studies are required to ascertain whether the catch-up growth may be at the expense of neurodevelopmental outcomes.

Future investigations will assess alterations in placental health/metabolomics in dams that survived AKI compared to sham or unmanipulated controls as a likely mechanism for the size discrepancy in the progeny.

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