

Functional implications of renal adaptations in gestational hypertension

Anita T Layton^{1,2} and Melissa M Stadt³

¹Departments of Applied Mathematics and Biology, University of Waterloo, anita.layton@uwaterloo.ca

²Cheriton School of Computer Science and School of Pharmacy, University of Waterloo,

³Department of Applied Mathematics and Biology, University of Waterloo, mstadt@uwaterloo.ca

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During pregnancy, major adaptations in renal morphology, hemodynamics, and transport occur to achieve the volume and electrolyte retention required in pregnancy. These changes are complex, and in isolation are sometimes counterintuitive. Additionally, during pregnancies complicated by gestational hypertension, altered renal function from normal pregnancy occurs. The goal of this study is to analyze how altered renal function during gestational hypertension impacts renal function during pregnancy. We hypothesize that hypertension-induced changes in renal transport pattern shifts Na^+ transport to downstream segments, while retaining sufficient K^+ for pregnancy needs. To test this hypothesis, we developed epithelial cell-based computational models of solute and water transport in the superficial and juxtamedullary nephrons of the kidney for a pregnant rat. Reductions in proximal tubule and medullary loop transporters are represented in the models. As a result, urine Na^+ and volume output are predicted to increase, which is evidence for pressure natriuresis. Due to differential changes in transporter activities, Na^+ transport load is predicted to shift to distal segments, where transporters are upregulated. Consequently, natriuresis and diuresis are partially counteracted. Simulation results also suggest that differential regulation of medullary (decrease) and cortical (increase) thick ascending limb transporters is important to preserve K^+ while minimizing Na^+ retention during gestational hypertension.

REFERENCES

- [1] M.M.Stadt and A.T.Layton, Adaptive Changes in single-nephron GFR, Tubular Morphology and Transport in Pregnant Rat Nephron: Modeling and Analysis, *Am. J. Physiol. Renal Physiol.*, 2021.
- [2] R. Hu, A. McDonough and A.T. Layton, Sex differences in solute and water handling in the human kidney: Modeling and functional implications, *iScience*, 102667, 2021.