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Presenting Author Category

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Research Category

Basic Science

Abstract Title

Investigating how in utero type 2 diabetes exposure affects kidney structure and function in offspring

Background

Exposure to maternal type 2 diabetes (T2D) has been shown to increase offspring risk for T2D and chronic kidney disease (CKD). However, it is unclear how maternal T2D exposure contributes to the pathophysiological changes in the kidneys of exposed offspring, making them more susceptible to CKD.

Objective

We hypothesized that exposure to maternal T2D impacts fetal development, leading to reduced nephron number, impaired glomerular function, and proximal tubular injury in the offspring, increasing susceptibility to CKD.

Methods

T2D was induced in female C57BL6 mice prior to pregnancy using diet-induced obesity (8-10 weeks of high-fat and -sucrose (HFS) feeding) and beta cell insufficiency (via injection of 75 mg/kg streptozotocin (STZ)). Control females were fed a chow diet and received a vehicle injection. Control and T2D females were mated with healthy males, and the offspring (males and females) were assessed for various aspects of kidney structure and function at 1- and 3-months of age.

Results

Urinary KIM-1 was significantly elevated in T2D-exposed offspring. Fewer glomeruli and thickened glomerular basement membranes without albuminuria were observed in T2D-exposed offspring. Male and female offspring showed similar findings.

Conclusion

T2D-exposed offspring experienced mild tubular injury, potentially impacting reabsorption of glucose, water and sodium. While in utero T2D exposure did not cause glomerular damage, the glomerular basement membrane thickening and reduced number of glomeruli suggest underlying changes that may increase kidney susceptibility to subsequent post-natal stress. Future studies exploring the responsible molecular mechanisms and characterizing how T2D exposure influences kidney function with subsequent post-natal stress are needed.

Authors

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