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Genomic Disorders, Chronic Kidney Disease and Neurocognitive Status in Children

Abstract

Children with CKD are at high risk for neurocognitive deficits compared to healthy age-matched controls. While cognitive deficits have been attributed to the burden of chronic illness, evidence demonstrates that deficits exist across a spectrum of CKD severity. Genome-wide analysis (GWAS) and copy number variant (CNVs) analysis has led to the identification of genetic loci associated with both isolated congenital anomalies of the kidney and urinary tract (CAKUT), as well as multiple developmental phenotypes, particularly cardiac or neurodevelopmental diseases. In addition to single-gene mutations associated with CAKUT, pathogenic CNVs have been detected in up to 16.6% of children with CAKUT and 7.4% of children with all-cause CKD. Studies have shown that neurocognitive deficits may be attributable to genomic disorders that simultaneously impair neurologic and kidney development. Genomic disorders have also been associated with developmental delay and neuropsychiatric disease. Our goal is to enroll 290 subjects 8 to 25 years of age with CKD to examine the link between CKD diagnosis, neurocognitive deficits and genomic disorders could be a potential explanation for these findings. We will pursue the following specific aims: 1) Identify genomic disorders in children with CKD; 2) Identify prevalence of neurocognitive deficits in children with CKD; 3) Assess the impact of return of genomic results on clinician and family knowledge and attitudes, and how does this affect decision-making.

The knowledge of associated neurocognitive deficits in affected patients with CKD could be invaluable for developmental and educational planning, which could positively affect the health outcomes for children with CKD.