# Cognitive Function in Children with Lupus Nephritis: A Cross-Sectional Comparison with Children with Other Glomerular Chronic Kidney Diseases

Andrea Knight, MD, MSCE[1,*], Amy J. Kogon, MD, MPH[2,*], Matthew B. Matheson, MS[3], Bradley A. Warady, MD[4], Susan L. Furth, MD, PhD[5], and Stephen R. Hooper, PhD[6]

**Objective** To identify factors contributing to cognitive impairment in children with lupus nephritis.

**Study design** A cross-sectional analysis of a large multicenter national cohort of children with chronic kidney disease (CKD) using standardized measures to determine baseline neuropsychiatric function and health-related quality of life (HRQoL) in children with lupus nephritis (n = 34), and to compare baseline function with that in children with other forms of glomerular CKD (gCKD; n = 171). We used inverse probability weighting via a logistic model for propensity score analysis to achieve balance between children with lupus nephritis and those with other glomerular causes of CKD, adjusting for known confounders. We used linear regression models to compare neurocognitive outcomes between exposure groups, adjusting for current prednisone use and testing for an interaction between current prednisone use and lupus nephritis, and to test for an association between cognitive function and HRQoL.

**Results** Current prednisone use was independently associated with worse attention ($P < .01$) and better adaptive skills ($P = .04$), and there was a significant interaction between current prednisone use and lupus nephritis for internalizing problems, with worse parent-reported internalizing problems in children with lupus nephritis on prednisone ($P = .047$). Better parent-reported HRQoL was associated with better visual memory ($P = .01$), and better child-reported HRQoL was associated with better attention ($P < .01$) and inhibitory control ($P < .01$). Both parent and child HRQoL were associated with better measures of executive function ($P = .02$ and $< .001$, respectively).

**Conclusion** Children with lupus nephritis have comparable or better cognitive function than their peers with other gCKDs, which is reassuring given the multiorgan and lifelong complications associated with lupus. *(J Pediatr 2017;189:181-8).*

Children with chronic kidney disease (CKD) are at risk for poor clinical and psychosocial outcomes because of kidney dysfunction, living with childhood chronic illness, and effects of treatments. Cognitive impairment in children with CKD is a known comorbidity, and studies indicate impaired function across several neurocognitive domains, including IQ, memory, and executive function.[1-3] Psychosocial functioning also may be adversely impacted in children with CKD, who suffer from higher rates of depressive and anxiety symptoms[4-8] and exhibit poorer health-related quality of life (HRQoL) compared with healthy peers.[9] Cognitive and behavioral dysfunction may adversely impact HRQoL, but little is known about this potential impact in children with CKD. Glomerular CKD (gCKD) may arise from several etiologies that may differentially impact cognitive and psychosocial functioning. Understanding these differences may yield insight into the pathophysiological mechanisms of cognitive and psychosocial dysfunction, as well as inform interventions to improve overall functioning and HRQoL in these children.

Fifty-five percent of children with systemic lupus erythematosus have gCKD,[10] and >20% exhibit moderate renal impairment by 10 years after diagnosis.[11] Children with lupus nephritis also may have central nervous system (CNS)

| | |
|---|---|
| BASC-2 | Behavior Assessment of Childhood Disorders, Second Edition |
| BRIEF | Behavior Rating Inventory of Executive Function |
| CKD | Chronic kidney disease |
| CKiD | Chronic Kidney Disease in Children |
| CNS | Central nervous system |
| CPT-II | Conners' Continuous Performance Test, 2nd Edition |
| D-KEFS | Delis–Kaplan Executive Function System |
| eGFR | Estimated glomerular filtration rate |
| gCKD | Glomerular chronic kidney disease |
| HRQoL | Health-related quality of life |
| WASI | Wechsler Abbreviated Scales of Intelligence |
| WIAT-II-A | Wechsler Individual Achievement Test, Second Edition, Abbreviated |
| WISC-IV-I | Wechsler Intelligence Scale for Children, Fourth Edition, Integrated |

From the [1]Division of Rheumatology, The Children's Hospital of Philadelphia, Philadelphia, PA; [2]Division of Nephrology, Nationwide Children's Hospital, The Ohio State University College of Medicine, Columbus, OH; [3]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; [4]Division of Nephrology, Children's Mercy Hospital, Kansas City, MO; [5]Division of Nephrology, Children's Hospital of Philadelphia, Philadelphia, PA; and [6]Department of Allied Health Sciences, University of North Carolina School of Medicine, Chapel Hill, NC

*Contributed equally.

The CKiD Study is supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases, with additional funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, and the National Heart, Lung, and Blood Institute (U01-DK-66143, U01-DK-66174, U01DK-082194, U01-DK-66116). The authors declare no conflicts of interest.

0022-3476/$ - see front matter. © 2017 Elsevier Inc. All rights reserved.

http://dx.doi.org10.1016/j.jpeds.2017.06.044

involvement, including neurocognitive impairment in up to 50%.[12-14] Inflammation of both the kidney and brain in children with lupus nephritis may exert concurrent adverse effects on cognitive and psychosocial function, and higher disease activity is associated with depression, anxiety, and poor HRQoL in these patients.[15,16] In addition, management of lupus nephritis carries a high burden of immunosuppressive medication use[17] and of psychosocial stress due to uncertainty resulting from the episodic nature of lupus and the potential for stigmatizing skin lesions.[18-21] Thus, children with lupus nephritis may have worse cognitive and psychosocial impairment than children with other forms of gCKD, but this has not been examined.

The Chronic Kidney Disease in Children (CKiD) prospective cohort study is a multicenter longitudinal investigation of children with mild-to-moderate CKD.[22] A primary goal of the CKiD study is to determine how a decline in kidney function affects neurocognitive function and behavior. As such, participants entered in CKiD undergo a battery of neurocognitive and behavioral tests, as well as repeated HRQoL assessments. Given the myriad of neuropsychiatric comorbidities associated with both CKD and lupus nephritis, we aimed to (1) determine whether children in the CKiD study with CKD secondary to lupus nephritis exhibit worse neurocognitive and psychosocial functioning and HRQoL compared with children with other forms of gCKD, and (2) examine the association of HRQoL with neurocognitive and behavioral functioning in children with lupus nephritis and other causes of gCKD.

## Methods

The CKiD study's design and objectives have been described previously.[22] Inclusion criteria include age 1-16 years and an estimated glomerular filtration rate (eGFR) between 30 and 90 mL/min/1.73 $m^2$. Exclusion criteria include renal or other solid organ, bone marrow, or stem cell transplantation, dialysis treatment within the past 3 months, HIV or cancer diagnosis or treatment within the past 12 months, structural heart disease, pregnancy within the past 12 months, genetic syndromes involving the CNS, and history of severe to profound intellectual disability. CKiD participants undergo standardized neurocognitive testing and assessment of psychosocial function at 6 months following study entry and then every 2 years after study entry. HRQoL is assessed at 6 months and at each annual visit thereafter. We used the baseline data (first visit with a measurement available) from these measures to determine the outcomes for this analysis. The CKiD study protocol was approved by the Institutional Review Boards at all participating sites, and informed consent and assent was obtained from all participants.

### Neurocognitive and Psychosocial Outcomes

The neurocognitive outcomes of interest included intelligence, measured by the Wechsler Abbreviated Scales of Intelligence (WASI)[23]; academic achievement, measured by the Wechsler Individual Achievement Test, Second Edition, Abbreviated (WIAT-II-A)[24]; memory, measured by the Digit Span Forward (verbal), Digit Span Reverse (verbal working), Spatial Span Forward (visual), and Spatial Span Reverse (visual working) portions of the Wechsler Intelligence Scale for Children, Fourth Edition, Integrated (WISC-IV-I)[24]; attention and inhibitory control, measured by the Detectability, Response Time Variability, and Errors of Commission subscores from the Conners' Continuous Performance Test, 2nd edition (CPT-II)[25]; and executive function, measured by the Global Executive Composite score from the Behavior Rating Inventory of Executive Function (BRIEF)[26] and the Achievement and Accuracy Ratio scores from Delis–Kaplan Executive Function System (D-KEFS) Tower Test.[27]

The WASI is a standardized measure of intelligence, and the WIAT-II-A is a standardized measure of academic achievement. Both tests are used for children aged ≥6 years and are reported as standardized scores with a mean of 100 and SD of 15; higher scores indicate better performance. The WISC-IV-I is a measure of intelligence that also measures discrete cognitive domains for children aged 6-16 years, with a mean of 10 and SD of 3; higher scores indicate better performance. The CPT-II measures attention, and the BRIEF is a parent-completed inventory that measures executive function. They are both validated for children aged ≥6 years and have a mean score of 50 and SD of 10; lower scores indicate better performance. The D-KEFS is for children aged ≥8 years and also measures executive function, with a mean score of 10 and SD of 3; higher scores indicate better performance.

Psychosocial outcomes of interest were assessed with the Behavior Assessment of Childhood Disorders, Second Edition (BASC-2), both parent- and self-reports,[28] and the PedsQL 4.0 HRQoL survey.[29] Both versions of the BASC-2 yield a total Behavioral Symptom Index Score and scores for the Externalizing Problems, Internalizing Problems, and Adaptive Skills indices. In addition, the child report yields the School Problems score. All scores on the BASC-2 have a mean of 50 and SD of 10. A higher score indicates better adaptive skills, and a lower score indicates worse behavioral symptoms, externalizing problems, internalizing problems, and school problems. HRQoL was assessed by the parent and self-report of the PedsQL 4.0. Domains of physical, emotional, social, school, and overall were measured. HRQoL scores range from 0 to 100, with higher scores indicating better HRQoL.

### Statistical Analyses

The primary outcomes of interest were the neurocognitive measures and BASC-2 and HRQoL scores. Descriptive statistics for the demographic, neurocognitive, BASC-2, and HRQoL variables were generated to characterize the study sample. For examination of differences in neurocognitive and psychosocial outcomes by disease group, the categorical exposure was lupus nephritis vs other gCKDs. To balance covariates between groups, we derived propensity scores from a logistic regression model containing the following variables: age, sex, height Z-score, race, ethnicity, maternal education, eGFR,[30] urine protein/creatinine ratio, systolic blood pressure Z-score, and anemia status. These variables were selected a priori to be likely risk factors and confounders for the outcomes. Three participants with unknown

Download English Version:

https://daneshyari.com/en/article/5718900

Download Persian Version:

https://daneshyari.com/article/5718900

Daneshyari.com