Depressive Symptoms in Children with Chronic Kidney Disease

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Objective To assess depression in children with chronic kidney disease and to determine associations with patient characteristics, intellectual and educational levels, and health-related quality of life (HRQoL).

Study design Subjects aged 6-17 years from the Chronic Kidney Disease in Children cohort study completed the Children's Depression Inventory (CDI), Wechsler Abbreviated Scales of Intelligence, Wechsler Individual Achievement Test-II-Abbreviated, and the Pediatric Inventory of Quality of Life Core Scales 4.0. Regression analyses determined associations of CDI score and depression status with subject characteristics, intellectual and educational levels, and HRQoL. A joint linear mixed model and Weibull model were used to determine the effects of CDI score on longitudinal changes in glomerular filtration rate and time to renal replacement therapy.

Results A total of 344 subjects completed the CDI. Eighteen (5%) had elevated depressive symptoms, and another 7 (2%) were being treated for depression. In adjusted analyses, maternal education beyond high school was associated with 5% lower CDI scores (estimate, 0.95; 95% CI, 0.92-0.99). Depression status was associated with lower IQ (99 vs 88; $P = .053$), lower achievement (95 vs 77.5; $P < .05$), and lower HRQoL by parent and child reports (effect estimates, −15.48; 95% CI, −28.71 to −2.24 and −18.39; 95% CI, −27.81 to −8.96, respectively). CDI score was not related to change in glomerular filtration rate.

Conclusion Children with depression had lower psychoeducational skills and worse HRQoL. Identifying and treating depression should be evaluated as a means of improving the academic performance and HRQoL of children with chronic kidney disease. *(J Pediatr 2016;168:164-70)*.

Depression is a common comorbidity in children with chronic medical disease[1-5] and has been associated with poor adherence to medication and worse outcomes.[4-6] Similar to children with other chronic diseases, children with chronic kidney disease (CKD) often experience growth restriction and multiple surgical scars, and frequently miss school and other childhood activities. Compared with previous decades, children with CKD are experiencing improved survival, but the adversities related to their underlying condition predispose them to developing depression. Compared with a 12-month prevalence of depression of 7.5% in adolescents in the general population,[7] previous studies assessing depression in pediatric CKD[6,8-12] have found a point prevalence of 10%-35%, with variations according to the specific populations studied (transplant vs dialysis vs pre–end-stage renal disease and young children vs adolescents) and methods used to define depression.

Although studies investigating the role of depression in pediatric CKD are limited, the role of depression in adults with CKD has been better defined. Studies in adults with CKD indicate a prevalence of depression of 20%-40%.[13-16] For adult patients on hemodialysis, major depression is associated with a 3- to 4-fold greater risk of death,[15] and those patients with CKD but not receiving dialysis have an increased risk of poor outcomes, including hospitalizations, death, and initiation of dialysis.[16] In pediatrics, adverse effects of depression are suggested by studies in adolescents in which depression is associated with neurocognitive impairment that improves after remission of depression[17] and in studies of children with chronic illness that show depression to be associated with poor quality of life.[18,19] These findings may be relevant in pediatric CKD, given that previous studies have found that 21%-40% of

CDI	Children's Depression Inventory
CKD	Chronic kidney disease
CKiD	Chronic Kidney Disease in Children
GFR	Glomerular filtration rate
HRQoL	Health-related quality of life
PedsQL	Pediatric Inventory of Quality of Life Core Scales 4.0
RRT	Renal replacement therapy

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children with CKD fall at least 1 SD below the mean on IQ and academic achievement[20] and have a lower health-related quality of life (HRQoL) than healthy children.[21]

The Chronic Kidney Disease in Children (CKiD) cohort study is a prospective observational study of pediatric patients with CKD and mild to moderate renal dysfunction from 54 pediatric nephrology centers throughout North America.[22] A primary goal of the study is to determine how a decline in kidney function affects neurocognitive function and behavior. Because previous studies evaluating depression in pediatric CKD are limited by small sample sizes (ranging from 15 to 60 subjects), and none has attempted to correlate depression with intellectual impairment, quality of life, or progression of disease, we used Children's Depression Inventory (CDI)[23] data collected from the CKiD cohort to determine: (1) the prevalence of depression and elevated depressive symptoms in children with mild to moderate CKD; (2) the demographic and clinical factors associated with depression in pediatric CKD; (3) the relationships between depression and intellectual level, academic skills, and quality of life; and (4) the relationship between baseline depression and longitudinal changes in kidney function.

Methods

The CKiD study is a multicenter prospective, longitudinal, observational cohort study of children with mild-to-moderate CKD from 54 pediatric nephrology centers throughout North America.[22] The study's design and objectives have been described in more detail previously.[22] The study was initiated in 2005 and enrolled children aged 1-16 years from a variety of pediatric nephrology practices with an estimated glomerular filtration rate (GFR) of 30-90 mL/min/1.73 m^2 (calculated by the original Schwartz equation[24]). Exclusion criteria included previous malignancy, transplantation, or dialysis within the previous 3 months, as well as a limited number of other conditions. Children were seen initially at a baseline study visit and then at another study visit 3-6 months later, at which point neurocognitive and psychosocial data were collected. Thereafter, subjects were followed longitudinally on an annual basis until age 21 years, they underwent transplantation, initiated dialysis, or were transferred to an adult center. This report includes subjects aged 6-17 years enrolled between 2005 and 2008, because these are the years of the study during which the CDI was administered, and only children at least 6 years of age completed the CDI. The CKiD study protocol was approved by the Institutional Review Board of each participating center, and informed consent was obtained from all participants.

We performed a cross-sectional analysis of data collected at baseline and at the 3- to 6-month study visit to determine the prevalence of depression and depressive symptoms and to examine the associations between depression and patient characteristics, intellectual function, overall academic skills, and quality of life. In a longitudinal analysis, we evaluated the relationship of CDI score to changes in GFR.

Depression

Participants completed the CDI at the 3- to 6-month study visit. The CDI is a validated 27-question survey designed to assess depressive symptomatology and to provide information regarding likely diagnoses of depression in children aged 7-17 years.[23] Children completed the CDI independently. For children who required help reading, the CDI was read to them by a study coordinator. The CDI assesses symptoms of depression in the domains of negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem. The results from the CDI yield a raw score, which is then converted into a T-score. The T-score is based on general population norms and standardized for age and sex, with a mean ± SD score of 50 ± 10 in the general child and adolescent population. A higher CDI T-score indicates the presence of more depressive symptoms; a CDI T-score ≥60 is considered high average, and a T-score ≥65 is considered clinically significant. For this study, depressed status was assigned based on a CDI T-score ≥60 or on a self-reported previous diagnosis of depression currently being treated with antidepressant medication. Depression was evaluated as a dichotomous outcome variable, and depressive symptoms were evaluated as a continuous outcome variable measured by CDI T-score.

Intellectual Functioning, Academic Achievement, and HRQoL Measures

All intellectual, academic, and quality of life measures were obtained concurrently with the CDI at the 3- to 6-month CKiD study visit. Intelligence was measured using the Wechsler Abbreviated Scales of Intelligence.[25] Academic achievement was measured with the Wechsler Individual Achievement Test-II-Abbreviated,[26] and the need for additional school support was assessed by self-reported presence of an individualized education plan or 504 Plan in the school setting. HRQoL was evaluated by completion of the Pediatric Inventory of Quality of Life Core Scales 4.0 (PedsQL).[27,28] Participants' caregivers completed the PedsQL parent proxy form, and participants aged ≥8 years completed the PedsQL child form.

Other Variables

Based on factors found to be associated with other neuropsychological measures in previous CKiD studies[20,21,29] we also collected data on age, sex, race, maternal education, etiology of CKD, age at diagnosis, duration of CKD, GFR, urine protein:creatinine, body mass index, height, casual blood pressure measurements, past history of psychiatric disease, and current medication use as variables possibly related to depression. For the cross-sectional analysis, demographic and medical history information was collected at the baseline study visit. For the longitudinal analysis, GFR was determined by plasma iohexol disappearance at the baseline visit, the first annual follow-up visit, and every 2 years thereafter.[30] At intervening visits, GFR was estimated by validated equations.[31] In this study, GFR refers to estimated GFR or measured GFR when available.