Kidney Medicine

The Burden of Mental Health Conditions in Children With CKD

Katherine L. Kurzinski and Darcy K. Weidemann

As medical advancements for children with chronic kidney disease (CKD) have led to improved long-term survival, appropriate recognition and treatment of the associated neuropsychiatric complications of CKD have become increasingly important. Recent studies examining the national trends of mental health disorders in children, particularly major depressive episodes and anxiety, confirm significant increases in the prevalence of these conditions in the general population.[1] Limited studies have shown a higher prevalence of psychiatric diagnoses in children with CKD, highlighting the importance of screening and characterization of mental health conditions in this patient group. A recent cross-sectional study of the Chronic Kidney Diseases in Children (CKiD) study by Stahl et al[2] in this issue of *Kidney Medicine* compared the prevalence of depression, anxiety, and attention-deficit/hyperactivity disorder (ADHD) in children across all stages of nondialysis CKD with that in children from the general population. The authors also evaluated the performance of a validated self-reported depression screening tool in comparison with parent-reported diagnoses, with some unexpected results.[2]

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In this study, investigators evaluated parent-reported diagnoses of depression, anxiety, or ADHD obtained at the study-entry interview from 875 children with CKD in the CKiD cohort from 2005-2015. They also examined comparable parent-reported diagnoses for the same 3 conditions from 72,699 individuals from the 2007 National Survey of Children's Health (NSCH). Using log-linear regression with Poisson distribution analysis, data were adjusted for age, sex, race, and ethnicity to provide adjusted prevalence ratios (aPRs) for depression, anxiety, and ADHD and ≥2 psychiatric diagnoses for children with CKD compared with the general population. Unsurprisingly, children with CKD had a higher prevalence of depression (crude prevalence, 5.7% vs 3.9%, respectively; aPR, 1.32; 95% confidence interval [CI], 1.01-1.73), while the adjusted prevalence of ADHD was similar between the CKiD and NSCH children (crude prevalence, 10.6% vs 9.2%, respectively; aPR, 1.03; 95% CI, 0.86-1.25). Perhaps the most unexpected finding of the study was a substantially lower prevalence of anxiety in children with CKD (crude prevalence, 4% vs 5.4% in the general population; aPR, 0.72; 95% CI, 0.52-0.99). The prevalence of multiple psychiatric diagnoses was also lower in children with CKD (crude prevalence, 3.1% vs 4.2% in the general population; aPR, 0.68; 95% CI, 0.47-0.99).[2]

The higher prevalence of depression in children with CKD is not surprising and is supported by the existing pediatric CKD literature, although the crude prevalence of 5.7% is lower than that observed in other studies, as summarized in Table 1.[2-9] Few prior studies included comparisons to healthy children and adolescents. A large-scale survey study showed a 12-month overall prevalence of depression in general US adolescents of 11.3%,[1] which differs somewhat from what was identified in the NSCH data, although differences in methodology may account for this. The ascertainment of neuropsychiatric diagnoses in the CKiD and NSCH study was quite similar, allowing for an appropriate comparison while minimizing bias, and represents a key strength of this study. This study's findings did not vary by CKD stage, sex, race and ethnicity, or maternal education status (although the aPR for depression was higher in females). Other studies have been mixed, with some showing no association of depression with the estimated glomerular filtration rate or CKD stage or severity and others demonstrating higher rates among those with later-stage CKD, including children receiving dialysis and after transplant.[4-6,8] One discordant finding within this study, however, was the lack of a correlation between the depression prevalence and maternal education level as noted in Kogon et al,[8] as individuals who met the Children's Depression Inventory (CDI) criteria for depression were more likely to have a mother with a high school education or less.

Among adults with nondialysis CKD, 1 study demonstrated an overall prevalence of depression of 21%.[10] Depressive symptoms are also described, with increased incidences in children with other chronic diseases, although the strength of this relationship varies by disease.[11] The true impact of depression in children with CKD remains unclear, but studies in children with kidney failure have shown lower adherence to treatment regimens and poorer health-related quality of life indices, while studies in adults with CKD show increases in dialysis initiation, hospitalization, and mortality.[8,12] Given this potential impact, it is imperative to screen for depressive symptoms in children with CKD to allow for timely interventions.

Interestingly, anxiety was found to be 28% less prevalent in children with CKD compared with the general pediatric population. Similar unexpected findings were noted in a smaller study by Kilicoglu et al[13] that described significantly lower mean state anxiety scores, using a validated anxiety inventory, in a cohort of 32 children receiving dialysis or with a kidney transplant compared with healthy controls. Also somewhat surprisingly, the authors noted a relatively equal prevalence of ADHD between both groups,

Table 1. Summary of Existing Data Comparing Prevalence of Depression, Anxiety, ADHD in Nondialysis Pediatric CKD Versus Control Populations

Study	CKD, n	Control, n	Crude Prevalence CKD (%)			Crude Prevalence Control (%)			Assessment Tool	Populations	Other Findings
			Depression	Anxiety	ADHD	Depression	Anxiety	ADHD			
Reynolds et al[3] (1991)	20	28	20	40	NA	4	14	NA	Birleson Scale parent report	Single center, age 3-18 (1983-1985, 1988-1989)	Evaluated ESKD, transplant recipients
Bakr et al[4] (2007)	19	NA	5.3	5.3	10.6	NA	NA	NA	SCICA DSM-IV	Single center, age 9-15 (2005-2006)	No correlation with age, sex, CKD duration, evaluated ESKD
Berney-Martinet et al[5] (2009)	20	40	35[a]	35	5	15.2	12.1	7.5	K-SADS-PL	Dual center, age 12-18 (2003-2004)	Evaluated transplant recipients
Kogon et al[6] (2013)	44	NA	30	NA	NA	NA	NA	NA	CDI-2	Single center, age 2-18 CKD III-ESKD (2011-2012)	Adjusted risk depression lower for duration (<3 y), advanced CKD
Moreira et al[7] (2015)	28	28	14.3	57.1	NA	0	50	NA	CDI SCARED	Single center, age 9-18 (2013)	Also evaluated Quality of Life scores
Kogon et al[8] (2016)	344	NA	7[b]	NA	NA	NA	NA	NA	CDI	CKiD, age 6-17 (2005-2008)	CDI unrelated to eGFR; depression lower in maternal education >HS
Kogon et al[9] (2019)	71	64	12	NA	NA	8	NA	NA	CDI-2	NiCK, age 8-25	Evaluated in 2 dialysis patients, depression associated with obesity
Stahl et al[2] (2022)	875	72,699	5.7	4	10.6	3.9	5.4	9.2	CDI parent report	CKiD, age 2-17 (2005-2015), NSCH (2007)	No correlation with eGFR, sex, age, maternal education, or race and ethnicity

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CDI, Children's Depression Inventory; CKD, chronic kidney disease; CKiD, Chronic Kidney Diseases in Children; DSM-KVIV, Diagnostic Statistical Manual of Mental Disorders; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HS, high school; K-SADS-PL, semistructured direct psychiatric interview; NA, not available; NiCK, Neurocognitive Assessment and Magnetic Resonance Imaging Analysis of Children and Young Adults With CKD Study; NSCH, National Survey of Children's Health; SCARED, Self-Report for Childhood Anxiety Related Disorders; SCICA, semistructured clinical interview for children and adolescents.

[a]Mood disorders, including major depression.

[b]Added together depressive symptoms and treated patients.

which is difficult to reconcile with the deficits in executive functioning and attention observed in the neurocognitive testing of even patients with mild CKD.[14] Biologically plausible mechanisms that provide a basis for increased ADHD and other neurocognitive deficits in children with CKD include low glomerular filtration rate affecting the normal neural pathway development, hypertensive effects on the developing brain, and attention variability noted in those with higher levels of proteinuria.[15,16]

Factors underlying this perplexing association remain unclear, although the authors postulate that the underreporting may be due to a variety of intentional and unintentional biases. Social desirability bias is plausible, wherein parents who may share a close relationship with their nephrology care team are less likely to report conditions perceived to be potential sources of stigmatization. An alternate hypothesis postulates underreporting because of state-wide differences in legislative protection for mental health conditions. The selection bias of children and families who agree to enroll in an intensive, longitudinal, prospective cohort study could also account for the differences observed. As the study period of CKiD enrollment spanned 10 years from 2005-2015, and the NSCH study was conducted in 2007, the possibility of a chronological bias because of changing prevalence rates of neuropsychiatric diagnoses over time should also be considered. The comparison of direct prevalence ratios with such a difference in time spans when the prevalence of these neuropsychiatric conditions is known to have increased substantially over the past few decades may need to be interpreted with caution. Finally, another interesting theory that deserves further exploration in future studies is the possibility that children with CKD are less likely to receive standardized, formal psychosocial screenings for these conditions because of delayed or absent preventative, well-child care visits through their primary care providers.

A secondary analysis by Stahl et al[2] examined pairwise correlations with parent-reported depression diagnosis data and clinically significant depressive symptoms on the CDI assessment. The CDI is a self-reported, previously validated assessment tool that is frequently used for the assessment of pediatric depression.[2,6,8,17] It has been adapted for use by the CKiD study, with data collected using this tool from 2005-2008 in children at least 6 years of age.[2,8,18] Surprisingly, parent-reported depression diagnosis data were weakly correlated with the CDI for clinically significant depression ($r = 0.13$; 95% CI, 0.03-0.23). The CDI identified clinically significant depression in only 6 of 346 patients in whom the survey was administered. In contrast, 24 of these patients had parent-reported depression but were negative by CDI criteria.[2]

A definitive depression diagnosis requires a comprehensive assessment by a qualified mental health professional, although this is a resource-intensive process that may not be feasible for large-scale epidemiological studies. Access to qualified mental health providers even for routine clinical care remains alarmingly poor. Although the CDI screening tool has been validated for use in clinical and nonclinical contexts for the identification of depression, 1 study showed poor performance and reduced sensitivity of CDI for depression in a population of 112 children with chronic illness.[19,20] Another, larger-scale meta-analysis questioned the sensitivity of CDI for depressive symptoms in chronic disease.[11] Conversely, parental awareness of mental health diagnoses may be affected by significant recall bias, thereby limiting its use. Further investigation into more accurate methods of depression screening when a comprehensive assessment is not feasible or validation studies of CDI in children with CKD seems warranted before future utilization of this tool because of the unacceptably low correlations observed in this study. As recognized by the study authors, a balance must be struck between efficient yet accurate psychiatric assessments in this vulnerable population. The use of longitudinal mental health assessments and the modification of existing study instruments to incorporate historical symptom data seem like worthy future directions for the research field.

Depression is more prevalent among children with CKD, and its adverse effects on patient outcomes are well described. Screening tools need to be optimized for identification and referral for treatment in this population to potentially improve CKD-related therapy adherence and reduce overall morbidity, and possibly mortality. Further evaluation of the true prevalence of anxiety and ADHD in children with CKD is warranted given the conflicting results in the current literature. The pervasiveness and impacts of mental health disorders in children with CKD are becoming more frequently recognized; thereby, formal, standardized screening programs and timely interventions should continue to be emphasized to provide optimal care for this vulnerable population.

ARTICLE INFORMATION

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Support: None.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Peer Review: Received March 22, 2022, in response to an invitation from the journal. Accepted April 14, 2022, after editorial review by the Editor-in-Chief.

 Published online May 2, 2022 with doi 10.1016/j.xkme.2022.100478

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