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Depression and its associated factors in pediatric chronic kidney disease

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Abstract

Background—Few studies on the occurrence of depression in pediatric patients with chronic kidney disease (CKD) have been conducted and none have identified associated clinical and demographic factors.

Methods—This was a cross-sectional study in which we administered the Child Depression Inventory-2 (CDI-2) to 44 patients aged 9–18 years with CKD stages III–V. Criteria for depression were CDI-2 scores of ≥ 65 or an established diagnosis of depression recorded in the medical chart. Relative risks (RR) and 95 % confidence intervals (CI) were calculated to determine associations between patient characteristics and depression status.

Results—Of the 44 patients enrolled in the study, 13 (30 %) met our criteria for depression, representing 18 % of patients aged <13 years and 34 % of those aged ≥ 13 years. Although not reaching statistical significance, the adjusted risk of depression was lower for patients with CKD duration of ≤ 3 years than for those with longer CKD duration (RR 0.19, 95 % CI 0.02, 1.53), and for those with CKD stage IV (RR 0.23, 95 % CI 0.05, 1.09) and CKD stage V (RR 0.13, 95 % CI 0.01, 1.07) compared to those with CKD stage III.

Conclusions—Our results indicate that depression is common in children with CKD, particularly for those with longstanding renal disease and at CKD stage III.

Keywords

Child depression inventory; Adolescents; Children; Dialysis; Transplant; Mental health

Introduction

As medical advances allow for the increased life expectancies of children with chronic kidney disease (CKD), the psychological complications of their disease become increasingly important. Children with CKD suffer from an illness that has no known cure and requires daily life-style modification. They often experience growth retardation and altered body image and frequently miss school and other normative activities, thereby affecting their psychosocial development [1]. These obstacles likely affect the psychological well-being of these children, but to date only a limited number of studies describe the mental health of children with CKD [2–7].

The prevalence of depression in the general child and adolescent population ranges from 0.4 to 8.3 %, with a higher prevalence reported in adolescents [8]. Studies in pediatric patients with chronic illnesses have shown that this patient population has a higher prevalence of depression than healthy populations and that depression has a negative effect on the underlying medical condition [2, 5, 9–13]. Studies of adults with CKD indicate a high risk of depression, with a prevalence between 20–40 % [14–17]. In adult hemodialysis patients, the occurrence of major depression is associated with a three- to fourfold greater risk of mortality [15]. Likewise, those not on dialysis have an increased risk of poor outcomes beyond that associated with other co-morbidities and kidney disease severity [16, 17]. However, despite the known adverse effects of depression on children with other chronic illnesses and on adults with CKD, few studies have investigated the occurrence of depression in children with CKD [2, 5]. Consequently, we have conducted a cross-sectional study to determine the prevalence of depression in pediatric patients with moderate to severe CKD and to identify patient characteristics associated with depression.

Methods

Study design and sample

Study subjects were recruited from the pediatric nephrology clinic at Seattle Children's Hospital, a tertiary care pediatric hospital serving as the referral center for the states of Washington, Alaska, Montana, and Idaho. All English- or Spanish-speaking patients with CKD stages III–V [estimated glomerular filtration rate (GFR) <60 ml/min/1.73 m², including those on dialysis and those with a renal transplant] between the ages of 7–18 years were eligible. Study visits occurred between 1 January 2011 and 29 February 2012. The study was approved by the Institutional Review Board of Seattle Children's Hospital and was therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All subjects provided written assent if 11–18 years of age or written informed consent if 18 years of age. One parent of each subject <18 years provided written informed consent.

Measurements of outcomes and variables

Clinical and demographic data for each subject were collected from his/her medical record at the time of the study visit. Current depression status was assessed by the Child Depression Inventory-2 (CDI-2), a questionnaire used to measure depressive symptoms and validated in children aged 7–17 years [18]. The subject completed the self-report version of the CDI-2,

and a parent completed the parent version of the CDI-2. The inventories were administered by paper and pencil format. The research assistant or principal investigator was available to answer questions and in some cases to read the inventory to the subject if necessary. For subjects in whom the primary spoken language was Spanish, the parent and subject had the option to complete the inventory in Spanish or English. All subjects completed the inventory in English; four parents completed the inventory in Spanish. Since the CDI-2 includes a question regarding suicidal ideation, any subject who reported suicidal ideation was assessed for safety by the nephrology social worker immediately after the study visit.

The self CDI-2 comprises 28 questions, and the parent CDI-2 comprises 17 questions. The questions assess symptoms in the domains of emotional problems (mood/physical symptoms, self-esteem) and functional problems (ineffectiveness and interpersonal problems). Each question is scored between 0 and 3 points, and all points are added up for a total raw score. The raw score is converted into a T-score ranging from 40 to 90 that is based on general population norms which are standardized for age and gender; the mean score $\pm$ standard deviation in the general child and adolescent population is 50 ± 10 . Scores obtained from the CDI-2 are then classified as a binary outcome, with a T-score of ≥ 65 consistent with a diagnosis of depression [18]. In our study, status as depressed or not depressed was assigned based either on scores ascertained from the parent or self CDI-2 or on a diagnosis of depression currently being treated as reported in the medical chart. The results from the parent CDI-2 were used to assess the presence of depression in subjects aged <13 years, and the results from the self CDI-2 were used in those subjects aged ≥ 13 years. CDI-2 subscale scores were also measured (emotional problems: mood/physical symptoms, negative self-esteem; functional problems: ineffectiveness and interpersonal problems).

The following patient characteristics were analyzed as categorical measures: gender; age (<13 year or ≥ 13 years); age at time of diagnosis (<5 years or ≥ 5 years); time since receiving a diagnosis of CKD (<3 years or ≥ 3 years); renal replacement status [pre-end stage renal disease (ESRD), dialysis or functioning transplant]; CKD stage at the time of study visit (stage III: GFR 30–59 ml/min/1.73 m²; stage IV: GFR 15–29 ml/min/1.73 m²; stage V: GFR <15 ml/min/1.73 m² or dialysis) (GFR was estimated using the bedside Schwartz equation [19] for subjects aged <18 years and by the Modification of Diet in Renal Disease Study Group equation [20] for subjects aged ≥ 18 years); height Z-score (<-1.5 and ≥ -1.5); body mass index (BMI) Z-score (<-1.5 and ≥ -1.5). Z-scores were used in the analysis to standardize measurements for age and gender. A change of one unit in the Z-score equals one standard deviation above or below the mean value for age and gender. Categorical measures were assigned to be clinically meaningful, i.e., age was categorized as child and adolescent, age at time of diagnosis was categorized according to age at which most children start formal schooling, and height and BMI Z-scores were categorized according to children who are of short stature and children who are obese.

For descriptive purposes, we collected information regarding the awareness of caregivers of a possible diagnosis of depression. The parents answered the following questions: (1) Have you ever been concerned that your child is depressed? (2) Have you ever spoken to your child's nephrologist about a possible diagnosis of depression? (3) Is there a family history of depression in mother, father, or sibling? (4) Is your child currently seeing a mental health provider? The subject's primary nephrologist answered the following question: Are you concerned about a diagnosis of depression in your patient?

Statistical analysis

Relative risks (RR) and 95 % confidence intervals (CI) were calculated to determine the associations between each characteristic and depression status. All relative risks were

adjusted for age and gender because both are known to be associated with depression in the general population [8]. Analyses were performed with STATA ver. 12.0 (StataCorp LP, College Station, TX).

Results

Sixty-seven eligible patients were identified and sent an informational letter about the study; 57 subjects subsequently attended a clinic visit in Seattle and were therefore approached about study participation; ultimately 44 (67 %) of the eligible patients completed the study. Reasons for eligible patient non-participation were related to conflicts between available study appointments and patient's availability in Seattle ($n=13$) and lack of interest ($n=10$). Non-participants and participants had a similar gender distribution, but non-participants were more likely to be CKD stage III and more likely to be of adolescent age (data not shown).

Characteristics of the participants are shown in Table 1. There were 20 pre-ESRD patients, 15 dialysis patients, and nine transplant patients. One patient with a functioning transplant was at CKD stage IV, and the remaining transplant patients were all at CKD stage III. The majority of the participants were of adolescent age and, following the expected demographics of pediatric CKD, the majority were male, diagnosed at a young age, and shorter than average height. Figure 1 displays the distribution of T-scores in our study sample according to the classification provided by the CDI-2. The distributions of CDI-2 scores in each measured subscale were similar to one another and to that of the overall depression scores. The sub-scale scores in all domains were significantly higher in the depressed patients than in the non-depressed patients ($p < 0.001$ for all comparisons).

Thirteen (30 %) subjects met study criteria for depression—ten based on the results from the CDI-2 and four based on a previous diagnosis of depression currently being treated. One patient met criteria under both definitions. Of the four subjects currently undergoing treatment, one had a CDI-2 score consistent with depression, while the other three scored in the normal range on the CDI-2.

Comparison of the parent to self CDI-2 scores revealed that four of the adolescents had scores indicative of depression on the self CDI-2 but not on the parent CDI-2. Seven of the adolescents not categorized as depressed because the self CDI-2 score was < 65 had a parent CDI-2 score indicative of depression. None of the children aged < 13 years had a self CDI-2 score indicative of depression, but two of them had a parent CDI-2 score indicative of depression and were therefore categorized as depressed.

Half of the subjects had a parent who, at some point, was concerned that his/her child was depressed, although fewer than half of the concerned parents (43 %) ever spoke about depression to the primary nephrologist (Table 2). Of the 13 subjects assessed as depressed 9 were currently seeing a mental health provider, although five of them reported that they did not carry a diagnosis of depression, were not taking antidepressant medications, and were unaware of undergoing any specific treatment for depression.

Table 3 shows the percentage of depressed patients by patient characteristic, with the adjusted relative risks and 95 % confidence intervals. Although all of the 95 % confidence intervals included the null and did not reach statistical significance, there are some notable trends in the data. The boys had a lower prevalence of depression than the girls (RR 0.68, 95 % CI 0.28, 1.70). Compared to adolescents, younger children had a lower prevalence of depression (RR 0.55, 95 % CI 0.15, 2.08). There was a suggestion of a lower risk of depression in those diagnosed with CKD after 5 years of age (RR 0.60, 95 % CI 0.22, 1.61)

and a lower risk in patients whose time since initial diagnosis of CKD was <3 years (RR 0.19, 95 % CI 0.02, 1.53). The patients on dialysis were less likely than the patients with pre-ESRD to be depressed (RR 0.38, 95 % CI 0.05, 2.91), and the patients with a functioning transplant were more likely than the pre-ESRD subjects to be depressed (RR 2.29, 95 % CI 0.91, 2.72). There was a negative association between depression and severity of CKD. Relative to the risk in patients with CKD stage III, the relative risk in patients with CKD stage IV was 0.23 (95 % CI 0.05, 1.09), and the corresponding relative risk among patients with CKD stage V was 0.13 (95 % CI 0.01, 1.07). Neither height nor BMI was associated with the prevalence of depression.

Discussion

Despite evidence that the presence of depression in children with chronic disease impacts the underlying medical condition [9–13], few studies describing the occurrence of depression specifically in children with CKD have been published. The 30 % overall prevalence of depression in our study indicates that depression is a common issue for children with CKD. To our knowledge, this is the first study to assess depression in pediatric CKD patients living in the USA and the largest study to identify the clinical and demographic factors associated with depression in this patient population.

Prior research conducted by Berney-Martinet et al. [5] assessed the lifetime prevalence of depression by clinical interview in 40 adolescent transplant patients and 20 adolescent pre-ESRD CKD patients living in Quebec, Canada. These authors found an overall prevalence of 35 %, which is comparable to the prevalence of depression in the adolescents in our study, but they did not seek to elucidate the associated factors. In a study conducted in Egypt in a cohort of pediatric CKD patients that included pre-ESRD CKD patients ($n=19$) and hemodialysis patients ($n=19$), Bakr et al. [4] assessed depression by clinical interview. These authors found a 10 % overall prevalence of depression, and although they attempted to study clinical and demographic factors associated with psychological disease overall, they did not comment on associations specifically with the depressed patients. They also mentioned that the presence of psychiatric disorders among their study cohort was not significantly correlated with age, sex, severity of anemia, duration of disease, or the efficacy of hemodialysis, but did not show the results on which they based this observation.

Similar to at least one study of depression in adult CKD patients, [14] we did not find that the likelihood of depression increased with worsening kidney function. Instead, the patients with less severe stages of CKD were more likely to be depressed. This suggests that depression may not be related primarily to the abnormal metabolic milieu of CKD patients. Rather, it is possible that due to different experiences with chronic disease, patients on dialysis have different life expectations that affect their moods and the perception of their disease. It is also possible that the lower intensity of medical services provided to patients with pre-ESRD CKD may affect their perceptions of psychological support. If this were to be the case, then providing more clinical and medical support to patients with less severe disease could be evaluated as a means of reducing depression. We must also consider the possibility of selection bias, since recruitment was lower among eligible patients in the CKD stage III group. Patients in this group with milder depressive symptoms may have differentially opted out of study participation.

In our cohort there was a higher prevalence of depression in those with a renal allograft than in those on dialysis and those who had pre-ESRD CKD. Since we did not assess the depression status of transplant patients with CKD stages I and II we were unable to determine if the high prevalence of depression in transplant patients in our study is related to deteriorating kidney function, to time with a diagnosis of CKD, or to something inherent to

the transplant process, such as poor adjustment to life with a transplant or neurotoxicity related to transplant medications. Interestingly, two small studies [5, 21] assessing the prevalence of depression in adolescent renal transplant patients found a similarly high prevalence of depression, but included transplant patients at all stages of CKD in their study population. The high prevalence of depression may be surprising given that transplantation is often viewed as the ideal treatment for ESRD, but it is of particular concern in pediatrics given the associations between depression and non-adherence [9] and the high rate of pediatric transplant graft loss that results from non-adherence [22]. Since depression may represent a modifiable risk factor for graft loss, the occurrence of depression in transplant patients should be further studied in a larger and more inclusive sample of patients.

Our data suggest that having a diagnosis of CKD for a longer time period may be associated with a higher likelihood of depression. This could indicate that over time the burden and stress of living with CKD increases and overwhelms a child's ability to adjust. A number of studies investigating depression in other pediatric chronic illnesses have, however, failed to find an association between depression and duration of illness [23, 24]. Understanding the extent to which time with a diagnosis of CKD affects the mental health of our patients will allow healthcare providers to determine when patients are most in need of psychosocial support and when interventions may be most effective.

Lastly, we assessed the awareness of caregivers about depression and whether parents were concerned about depression in their children. We found that fewer than half of the parents who were concerned that their child was depressed have ever spoken to the primary nephrologist about their concern and that a primary nephrologist's concern for depression in a patient is usually well founded. Despite the concerns of caregivers and professionals, only four of the 13 depressed children in our study were identified by their parents as carrying a diagnosis of depression and being treated for it. This number reflects a general problem of under-recognition and undertreatment of depression in pediatric patients [25, 26] and should serve as a reminder of the need to assess depression and overcome barriers to depression treatment. To overcome these barriers, we need to determine if they are due to a lack of knowledge about the evidenced based behavioral treatments for depression that are available (such as cognitive behavioral therapy), concerns about children with CKD using psychotropic medications, misconceptions of patients and physicians regarding the need for depression treatment, or lack of time to prioritize depression screening and treatment in an already overly busy medical schedule.

Our study was limited by a small sample size in a single pediatric center, which led to statistical uncertainty for most of the associations we observed. Furthermore, due to the sample size, many important facets of depression were not included in our analysis. Understanding the interplay between factors such as quality of life, level of family functioning, socio-economic status, and social support could be important.

Finally, our use of the CDI-2 to measure depression, rather than a diagnostic interview, may have introduced some misclassification of depression. The CDI-2 has not been validated in the pediatric CKD population, a population in which fatigue, insomnia, anorexia, and psychomotor retardation are common clinical features. Despite this, we used the CDI-2 since it is based on the *Diagnostic and Statistical Manual of Mental Disorders* [27], is easy to administer and interpret, and is validated in the general pediatric population (sensitivity and specificity 83.2 and 73.3 % respectively [18]). On evaluation of our data, it is unlikely that physical symptoms were misrepresented as depressive symptoms since the sub-scale scores in all domains were significantly higher in the depressed patients than in the non-depressed patients, and the highest average subscale score in the self-report (mean score 64) was in functional problems, a scale that does not incorporate physical symptoms. Further

evidence of the CDI-2 differentiating the depressed from non-depressed subjects were the responses to the item regarding suicidal ideation. None of the non-depressed subjects responded positively to the CDI-2 item that they think about killing themselves or want to kill themselves, whereas five of the 13 depressed subjects responded positively to one of these suicidal ideation items.

There is evidence to suggest that depression plays an important role in the trajectory of chronic disease. In both pediatric chronic illness and in adult CKD, depression is associated with worse long-term outcomes [9–13, 15–17]. This study suggests that a high proportion of children with CKD are depressed and that those with a diagnosis of kidney disease for >3 years and those with CKD stage III may be particularly susceptible. This study raises important questions for future studies to explore in an attempt to reduce the burden of depression in this patient population and to improve the outcomes of pediatric CKD.

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Fig. 1. The number of patients who scored within certain ranges on the Child Depression Inventory-2 (CDI-2). Scores of 65 are consistent with a diagnosis of depression

Table 1

Characteristics of subjects at time of study visit

Characteristic	Values (n) or median [IQR]
Gender	
Female	30 % (13)
Male	70 % (31)
Age (years)	14 [12.5, 16.5]
9–12	25 % (11)
13–18	75 % (33)
Race	
Non-Hispanic white	71 % (30)
Hispanic	29 % (12)
Black	2 % (1)
Unknown	2 % (1)
Age at time of diagnosis of CKD (years)	1.3 [0,12]
0–5	57 % (25)
6–18	43 % (19)
Time since diagnosis of CKD (years)	11 [3,15]
0–3	25 % (11)
>3	75 % (33)
Renal replacement status	
Pre-ESRD	45 % (20)
Dialysis	34 % (15)
Functioning transplant	20 % (9)
CKD Stage	
CKD stage III	34 % (15)
CKD stage IV	30 % (13)
CKD stage V	36 % (16)
Height Z-score ^{a,b}	−0.56 [−1.14,0.05]
−1.5	19 % (8)
>−1.5	81 % (35)
BMI Z-score ^{a,b}	0.2 [−0.72, 1.16]
1.5	86 % (37)
>1.5	14 % (6)

CKD, Chronic kidney disease; ESRD, end-stage renal disease; BMI, body mass index

Data in table are presented as the percentage with the number in parenthesis or as the median with the interquartile range between square brackets

^a A change of 1 unit in the Z-score equals one standard deviation above or below the mean value for age and gender

^b One patient did not have a height measured: Z-score could not be calculated

Table 2

Caregiver concern about possible depression

Caregiver concern	Total <i>n</i> (% of total cohort)	Depressed <i>n</i> (% of row total)	Not depressed <i>n</i> (% of row total)
Parent concerned child is depressed	22 (50)	9 (41)	13 (59)
Parent spoke to nephrologist about concern child is depressed	19 (43)	10 (53)	9 (47)
Primary nephrologist concerned child is depressed	9 (20)	6 (67)	3 (33)
Family history of depression in first-degree relative	21 (50)	8 (38)	13 (62)
Currently seeing mental health provider	13 (31)	9 (69)	4 (31)

Table 3

Correlates of depression in pediatric patients with chronic kidney disease (CKD)

Characteristic	<u>Depressed</u>		RR ^a	95 % CI
	<i>n</i>	%		
Gender				
Female	5	38	Reference	Reference
Male	8	26	0.68	0.28, 1.70
Age (years)				
9–12	2	18	0.55	0.15, 2.08
13–18	11	34	Reference	Reference
Age at time of diagnosis of CKD (years)				
0–5	9	36	Reference	Reference
6–18	4	21	0.60	0.22, 1.61
Time since diagnosis of CKD (years)				
0–3	1	9	0.19	0.02, 1.53
>3	12	36	Reference	Reference
Renal replacement status				
Pre-end stage renal disease	5	25	Reference	Reference
Dialysis	2	13	0.38	0.05, 2.91
Functioning transplant	6	67	2.29	0.91, 2.72
CKD stage				
CKD stage III	9	60	Reference	Reference
CKD stage IV	2	15	0.23	0.05, 1.09
CKD stage V	2	13	0.13	0.01, 1.07
Height Z-score ^b				
–1.5	2	25	0.92	0.25, 3.36
>–1.5	10	29	Reference	–Reference
BMI Z-score ^b				
<1.5	11	30	Reference	Reference
1.5	2	29	0.78	0.16, 3.87

^aRR adjusted for age and gender^bOne patient did not have a height measured and so the Z-score could not be calculated