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ORIGINAL ARTICLE

Anxiety, depression, resilience and quality of life in children and adolescents with pre-dialysis chronic kidney disease

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Abstract
Background Chronic kidney disease (CKD) is a risk factor for psychosocial impairment and psychiatric symptoms. Children and adolescents on dialysis frequently have compromised daily life activities and a worse quality of life (QoL) compared with healthy peers. However, few studies have investigated these aspects of CKD in pediatric pre-dialysis CKD patients. Therefore, we have analyzed resilience, QoL and anxiety and depressive symptoms in children and adolescents with pre-dialysis CKD and compared these to the values of healthy controls.
Methods Demographic and clinical data were collected from 28 children and adolescents with pre-dialysis CKD and 28 healthy sex- and age-matched controls. Psychological assessment of the participants was performed using the Wagnild and Young Resilience Scale, Pediatric Quality of Life (QoL) Inventory 4.0 , Child Depression Inventory and Self-report for Childhood Anxiety Related Disorders scales.
Results Of the 56 children enrolled in our study, the CKD patients were referred to mental health professionals more frequently than the controls. Patients exhibited higher scores for separation anxiety and a higher frequency of clinically significant depressive symptoms. They also had lower overall QoL scores, as well as poorer scores for the psychological, educational and psychosocial subdomains of QoL instruments. There was a negative correlation between anxiety and depressive symptoms and all domains of QoL. Resilience was similar in both groups, but lower in patients with significant depressive symptoms. No significant association was found between clinical or laboratory findings and psychological variables in CKD patients.
Conclusion Although patients and controls exhibited similar scores of resilience, CKD negatively impacted the QoL of pediatric patients, contributing to a higher frequency of depression and separation anxiety.

Keywords Quality of life · Resilience · Psychiatry · Chronic kidney disease · Pediatric

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Introduction

Chronic kidney disease (CKD) is characterized by progressive renal injury with inevitable functional deterioration. This functional loss is usually slow, progressive and irreversible [1]. The frequency of end-stage renal disease (ESRD) in the Brazilian pediatric population is still uncertain, but the authors of a study conducted in São Paulo reported 23.4 cases of ESRD per million children and adolescents [2]. However, pre-dialysis stages of CKD still remain underdiagnosed and underestimated in pediatric patients since most data sources rely on information gathered from dialysis and/or transplant centers [2, 3].

CKD can profoundly influence the daily routines of pediatric patients and their families, requiring significant social adaptation by both patient and family [4]. Ideally, the management of CKD in children and adolescents requires a multidisciplinary team [1]. Although marked therapeutic advances have been made in recent years, CKD can be especially devastating to the pediatric patient because of its high mortality

rate (up to 30-fold higher than that of same-age children in the general population) [5] and frequent hospitalizations, with significant impairment of health-related quality of life (HRQoL) [4, 6]. Despite the limited information currently available in pediatric CKD, research has confirmed that HRQoL is generally compromised, with CKD patients scoring lower than their healthy peers [4, 6–8]. However, Varni and co-workers reported that children with ESRD exhibited better emotional scores of HRQoL than children with other chronic diseases, including diabetes, asthma, cerebral palsy and cardiac and rheumatologic diseases [9].

The behavioral response to chronic diseases in childhood and adolescence has been studied over the past years, with somewhat conflicting results [10–14]. Meta-analyses have confirmed an increased risk for overall adjustment disorders in these children and adolescents [10, 11], with impaired development of self-concept or self-esteem and an elevated prevalence of externalizing (e.g. hyperactivity or aggression) or internalizing symptoms, such as anxiety, social withdrawal and depression [10, 11]. Accordingly, screening for psychiatric symptoms and signs of psychological distress should be a concern of pediatric health practitioners and others working with children with chronic illnesses [10]. CKD studies in the pediatric patient population have found an elevated frequency of psychiatric disorders, with the most commonly observed disorders being adjustment disorders, depressive symptoms, anxiety and cognitive impairment[4, 12–14]. However, the association between clinical or laboratory features, disease duration and severity and psychological variables remains undetermined [4, 10–14].

The concept of resilience has emerged from studies on successful adaptation despite challenging or threatening circumstances [15]. The first subjects of such studies were children who had been exposed to stressful environments or traumatic events and who had, theoretically, a higher risk for developing psychopathological conditions but who had managed to overcome related difficulties. Therefore, resilience refers to an adaptive behavior associated with either internal states of well-being or adequate functioning in the environment and can be also defined as "a dynamic, multidimensional process, which results in positive adaptation in adverse contexts" [16]. Resilience in the context of CKD is much less investigated. Ma et al. [17] found that pre-dialysis adult patients had lower scores of resilience than newly diagnosed CDK patients and high-risk individuals (families of CKD patients) and that resilience positively correlated with health-promoting behaviors. Lee et al. [18] reported that hemodialysis patients with more depressive symptoms had lower resilience scores in the Hamilton Depression Rating scale. In their 2007 multi-center study, Varni et al. [9] used the Child Health and Illness Profile—Adolescent Edition (CHIP-AE) to assess resilience in children with CKD. The resilience domain of the CHIP-AE consists of the subdomains Family Involvement, Physical Activity, Social Problem-solving, and Home Health and Safety, and the higher the score, the better the functioning of the patient for that subdomain. CKD patients scored higher than the control group of healthy adolescents in the subdomain Home Health and Safety and did not differ in their total score from the controls. Dialysis patients scored lower than pre-dialysis and post-transplant patients [9]. To our knowledge, there are no studies that have evaluated resilience in children and adolescents with pre-dialysis CKD using specific resilience scales. The last report of the National Institutes of Health task force on research priorities in CKD in children pointed out the need for research into secondary prevention of depression in children and their parents and into the contribution of education and lifestyle, together with methods to facilitate rehabilitation, maximize educational experience and assess self-esteem and self-worth [19].

The aim of this study was to investigate resilience, QoL, anxiety and depressive symptoms in children and adolescents with pre-dialysis CKD and compare these values to those of healthy controls. Our hypothesis was that pre-dialysis CKD children and adolescents are at risk for a lower HRQoL and for psychiatric disorders, with higher morbidity possibly related to disease duration or severity, as well as to other clinical or laboratory variables. The capacity for resilience, on the other hand, would be a protective factor. The identification of comorbidities in children with CKD could help decrease the burden of CKD.

Methods

Study design

This cross-sectional study included 28 pediatric pre-dialysis CKD patients (stages 1–4) followed-up at the Pediatric Nephrology Unit, UFMG University Hospital, from June to December 2013 and 28 healthy controls who were age- and sex-matched, from public schools located in the same geographic area. Diagnostic criteria for CKD were based on the National Kidney Foundation's Kidney Disease Outcomes Quality Practice classification [20].

The local Ethics Committee evaluated and approved this study. Informed consent was obtained from all parents, CKD patients and healthy controls included in the study. The research protocol did not interfere with any medical recommendation(s) or prescriptions.

Inclusion and exclusion criteria

CKD patients All CKD children and adolescents at CKD stages 1–4 who were followed-up at UFMG University Hospital from June to December 2013 and for whom an informed consent form was obtained were eligible for enrolment in the

study. Patients with acute illness (e.g. infections, clinical instabilities or glomerular disease activity) were not scheduled for interviews during the period of the acute illness or disease activity. Literate individuals of both sexes, regardless of socioeconomic status, were included. The age of the patients ranged from 9 to 18 years. Exclusion criteria were hearing impairment, writing or reading disabilities and previous diagnosis of intellectual disability or autism spectrum disorders (eight patients were excluded and three refused to participate).

Controls The control group consisted of healthy sex- and age-matched children from public schools who gave informed consent to take part in the study. All controls were normotensive and had no medical or family history of renal diseases. Healthy status was determined through a review of the medical history and either a parental report or self-report to rule out the presence of chronic or acute diseases. Subjects with hearing impairment, writing or reading disabilities and a previous diagnosis of intellectual disability or autism spectrum disorders were excluded.

Study protocol

After informed consent had been provided, CKD patients, controls and their parents were asked to complete several psychometric instruments that are designed for evaluation of anxiety, depressive symptoms, HRQoL and resilience, as detailed in the section Demographic and psychological assessment. Clinical and laboratory data were already available as part of the routine protocol for managing CKD patients at our unit, as described in detail elsewhere [1, 21]. Medical visits were scheduled at intervals of approximately 3 months, and a complete physical examination and battery of laboratory tests were repeated on each occasion. Glomerular filtration rate (GFR) was estimated (eGFR) adopting the original Schwartz formula [22]. Associated conditions were managed as per our unit protocol. Supplements of electrolytes, vitamin D and erythropoietin were given according to standard recommendations [23, 24]. Blood pressure was classified according to the Fourth Task Force guidelines [25], and antihypertensive drugs were used for patients with blood pressure persistently above the 95th percentile.

Clinical and laboratory measurements

Clinical characteristics, anthropometric measurements and laboratory test results were evaluated during the clinic visit and by reviewing medical records at the time of interview. Clinical data included gender, age, height, weight, body mass index, etiology and stage of CKD and the presence of hypertension.

Laboratory tests included serum levels of creatinine, hemoglobin, albumin, cholesterol, triglycerides, total calcium, phosphorus, bicarbonate, parathormone and uric acid; in addition, the ratio between protein and creatinine in spot urine was analyzed. GFR was calculated by Schwartz's equation [22] to classify CKD stage [20].

Demographic and psychological assessment

Demographic data were collected by interview with the parents or caregivers of the patients and controls. Delayed educational attainment was defined as an inadequate correspondence between the subject's age and school level.

All psychometric instruments used for psychological assessment were read to the participants to reduce differences due to educational levels and performance.

Resilience The Wagnild and Young Resilience Scale [26] was used to evaluate resilience. This instrument has been validated by Pesce et al. [27] for Brazilian adolescents. It contains 25 affirmative items with a Likert-type scale response from 1 (strongly disagree) to 7 (strongly agree). The scores range from 25 to 175 points, with higher values indicating higher resilience.

Quality of life We used the Pediatric Quality of Life Inventory 4.0 (PedsQL^{TM}; referred to further in text as the PedsQL) to evaluate the QoL. This instrument was designed by Varni et al. [28] with the aim to measure HRQoL as outlined by the World Health Organization. It consists of 23 items, which are inversely scored and subsequently translated to a scale of 0–100, meaning that the higher the score the better the QoL. It was validated in Brazil by Klatchoian et al. [29]. The results assess physical and psychosocial dimensions in four multidimensional subscales, namely, physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and school functioning (5 items), and measures a total (global) scale (23 items) score and psychosocial (15 items) score.

Psychiatric symptoms

- **Child Depression Inventory (CDI):** This instrument is an adaptation of the Beck Depression Inventory which is based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria. CDI was developed by Kovacs [30] to screen young people (age 7–18 years) for depressive symptoms. It is composed of 27 items with three possible responses, scored from 0 to 2. The cut-off point of 18 has been used for the Brazilian population [31].
- **Self-report for Childhood Anxiety Related Disorders (SCARED):** This instrument was designed by Birmaher et al. [32] to screen for symptoms of anxiety. It consists of 41 items, and five subscales or factors, which are in correspondence to DSM-IV anxiety disorders. Each item has three options of answers, with scores of 0 (never or almost never), 1 (sometimes) or 2 (often). Total scores can

range from 0 to 82. It can also be scored per subscale: panic/somatic, generalized anxiety, separation anxiety, social phobia and school phobia. The total cut-off point for the Brazilian population was set at 22 [33].

Statistical analysis

The software Statistical Package for Social Sciences (SPSS) version 16.0 (Chicago, SPSS Inc, 2007) was used for statistical analysis. Values were expressed as the median and range (minimum and maximum values) or as the mean and standard deviation, where appropriate. Dichotomous variables were expressed as numbers and percentages and compared using the chi-square test. The normality of the distribution was evaluated by the Shapiro–Wilk test and histogram for each group. The unpaired Student's *t* test was used to compare means when normally distributed variables were assessed, while the Mann–Whitney and Kruskal-Wallis tests were used to compare medians between two and three or more groups, respectively. The analysis of dichotomous variables was performed using the chi-square test. The Spearman test was used to evaluate correlations. The level of significance was set at $p<0.05$.

Results

CKD patient characteristics

In CKD patients the average disease duration was 11.7± 3.3 years, which was very similar to the duration of treatment or follow-up (11.0±3.3 years). The majority of CKD patients (67.9 %) were prescribed anti-hypertensive drugs. Only one patient was using a psychotropic drug (fluoxetine 10 mg) which had been prescribed due to overweight. Two patients (7 %) were hospitalized in the previous year. In terms of the causes of CKD in our patient population, the most predominant were congenital anomalies of the kidney and urinary tract (CAKUT) (50 %), followed by glomerular diseases (17.9 %), cystic diseases (10.7 %) and other causes (21.4 %). Regarding the stage of CKD, six patients were at stage 1 (21.4 %), seven at stage 2 (25 %), eight at stage 3 (28.6 %) and seven at stage 4 (25 %). Clinical and laboratory features are shown in Table 1.

When patients were grouped according to stage of CKD, there was no difference among subgroups in terms of age, disease or treatment duration, number of medications in use and SCARED, CDI, PedsQL™ and resilience scale scores. There was also no difference when patients with CKD stages 1 and 2 were combined and compared to those with stages 3 and 4 combined. There was no significant correlation between the psychological variables and either laboratory values or eGFR (data not shown).

Demographic factors

Children and adolescents with CKD did not differ from controls in terms of age, sex or school attendance (Table 2). However, there was a significant difference in the frequency of grade retention ($p<0.001$), delayed educational attainment ($p<0.001$) and interruption of studies ($p=0.004$), with 32 % of CKD patients having interrupted their studies at some point (for an average of 4.8 months), among whom 44.4 % attributed this interruption to CKD or its treatment. Sixteen (57 %) children and adolescents with CKD were delayed in school. There was also a difference regarding a history of previous psychiatric or psychological treatment(s), which had occurred in ten patients with CKD (35.7 %) compared to only one of the controls (3.6 %) ($p=0.002$).

Resilience and QoL

The resilience scores did not differ between patients and controls (Table 3). In the univariate analysis, resilience was not associated with grade retention, delayed educational attainment or interruption of studies. Resilience also did not correlate with either the years of schooling or the length of school absenteeism. The univariate analysis did reveal an association between lower scores of resilience and clinically significant depressive symptoms (Table 4). There was no significant correlation between resilience and other psychological scores in CKD patients, whereas, in the control group, resilience was negatively correlated with CDI score ($r=-0.496$, $p=0.007$).

The results for HRQoL were significantly lower in the group of CKD patients for the global, psychological, educational and psychosocial dimensions of the PedsQL. Surprisingly, QoL scores did not significantly differ in the physical dimensions (Table 3). In CKD patients, male sex was associated with impaired social HRQoL ($p=0.027$; Table 4). Previous psychiatric treatment was associated with worse HRQoL scores. There was no difference in terms of adequate education or interruption of studies due to illness.

Anxiety and depression

Anxiety and depressive symptoms in CKD patients and controls are shown in Table 5. There was no difference between the scores of global anxiety and depressive symptoms among children and adolescents with CKD and controls. For the SCARED subscales, CKD patients showed higher scores only in the subscale separation anxiety ($p=0.018$). When subjects were categorized based on each subscale's cut-off score, children and adolescents with CKD exhibited higher frequencies of clinically significant depressive symptoms ($p=0.04$) compared to controls. On the other hand, clinically significant anxiety was similar in both groups. In the control group, girls showed more symptoms in the panic subscale ($p=0.029$).

Table 1 Clinical characteristics, etiology of chronic kidney disease (CKD), CKD stages and laboratory values of children and adolescents with predialysis CKD

Patient demographic and clinical characteristics	Values[a]	Minimum and maximum values	Laboratory values	Values[a]	Minimum and maximum values
Demographic parameters					
Height (cm)	156.3±13.2	130–175	Creatinine (mg/dl)	2.3±1.5	0.8–6.4
Height <5th percentile	7 (25)		Urea (mg/dl)	141.5±2.9	136–146
BMI (body mass index)	19.2±4.9	14.7– 29.6	Total calcium (mg/dl)	9. 6±0.7	7.7–10.8
BMI <5th percentile	7 (25)		Phosphorus (mmol/l)	5.1±0.9	3.1–8.2
BMI >5th percentile	2 (7.1)				
Blood pressure >5th percentile	4 (14.2)		Parathormone (pg/ml)	174±168	16–652
Use of antihypertensive drugs	19 (67.9)		pH	7.32±0.04	7.23–7.40
Number of medications in use	3.8±1.6	1–6	Bicarbonate (mmol/l)	23.3±2.8	17.8–27.7
Disease duration (years)	11.7±3.3	5–17	Presence of acidosis	21 (75 %)	
Treatment duration (years)	11.0±3.6	4–15	Hemoglobin (g/dl)	11.9±1.9	7.6–15.3
CKD etiology			Presence of anemia	7 (25 %)	
Congenital anomalies of the kidney and urinary tract	14 (50)		Uric acid (mg/dl)	6.8±1.4	4.4–9.6
Glomerulopathies	5 (17.9)		Total cholesterol (mg/dl)	157±29.4	107–211
Renal cystic diseases	3 (10.7)		Low-density lipoprotein (mg/dl)	84.3±29	40–139
Other causes	6 (21.4)		High-density lipoprotein (mg/dl)	53.4±22	31–105
CKD stage			Triglycerides (mg/dl)	91.0±35.2	42–179
Stage 1	6 (21.4)				
Stage 2	7 (25)				
Stage 3	8 (28.6)				
Stage 4	7 (25)				
Glomerular filtration rate (ml/min/1.73 m^{2b})	56±28	10–85			

BMI, Body mass index

[a] Continuous variables are expressed as mean±standard deviation (SD) and as minimum-–maximum values. Categorical variables are shown as number of cases with the percentage given in parenthesis.

[b] Glomerular filtration rate (GFR) is estimated by Schwartz formula [22]

Depressive and anxiety symptoms negatively correlated with all domains of HRQoL (r values varying from −0.385 to −0.652, with p values ranging from 0.001 to 0.043, and r values varying from −0.399 to −0.748, with p values ranging from 0.001 to 0.035). Disease duration negatively correlated with psychosocial, psychological and school domains of PedsQL ™ (r values varying from −0.444 to 0.586, with p-values ranging from 0.001 to 0.026) and positively with the scores of CDI (r=0.425, p=0.027) and SCARED (r=0.404, p=0.037).

Discussion

The aim of this study was to investigate resilience, HRQoL, anxiety and depressive symptoms in pediatric CKD patients and to compare the scores of this patient group to those of age- and sex-matched healthy peers. Since studies focusing on predialysis CKD in children and adolescents are scarce, the evaluation of this population is important for delineating more effective interventions to alleviate disease burden. In our study, children and adolescents with CKD had lower scores for HRQoL in comparison to the controls, regardless of their clinical severity. Depressive and anxiety symptoms negatively influenced HRQoL perception. Moreover, lower resilience scores were associated with clinically significant depressive symptoms.

In terms of the main causes of CKD, our sample was comparable to those of previous studies with the same age interval [4, 9]. The overlap of disease and treatment duration may also reflect the higher frequency of congenital and hereditary abnormalities in our sample.

We found a significant difference in the frequency of grade retention, delayed educational attainment and interruption of studies between CKD patients and matched controls. This high frequency of patients with delayed educational attainment may be indicative of possible cognitive impairment related to CKD [34]. It is worth mentioning that cognitive

Table 2 Social, demographic and educational characteristics of the pediatric patients with chronic kidney disease (CKD) and the controls

Social, demographic and educational characteristics	CKD patients	Controls	*p*
Age (years)	13.7±1.8	14.2±1.1	0.92
Median (range)	14.0 (9–17)	14.0 (13–17)	
Sex			
Female	10 (35.7)	13 (46.4)	0.42
Male	18 (64.3)	15 (53.5)	
Place of residence			
Urban	25 (89.3)	25 (89.3)	1.0
Rural	3 (10.7)	3 (10.7)	
Years of schooling	6.4±2.0	7.4±1.0	0.05
Median (range)	7.0 (3–10)	7.0 (6–11)	
Delayed educational attainment	16 (57.1)	2 (7)	<0.001
Grade retention	16 (57.1)	2 (7)	<0.001
Study interruption	9 (32.1)	1 (3.5)	0.004

Continuous variables are expressed as the mean± SD and as the median with the minimum and maximum values in parenthesis. Categorical variables are shown as number of cases with the percentage given in parenthesis

Table 3 Scores of resilience and quality of life (Peds-QL^{TM}) in children and adolescents with chronic kidney disease (CKD) and the controls

Scores of resilience and quality of life (Peds-QL^{TM})	CKD patients	Controls	*p*
Resilience, mean±SD	119.3±25.0	127.6±19.1	0.171
Median (range)	120.8 (54–148)	129.0 (79–155)	
Quality of life total score and subdomains			
PedsQL—Total (Global)	73.1±13.4	81.7±9.7	0.008
Median (range)	70.2 (39.1-93.5)	83.0 (65.2-100)	
PedsQL—Physical	75.7±17.4	85.8±13.1	0.055
Median (range)	78.1 (31.3-100)	90.6 (50–100)	
PedsQL—Psychological	61.6±19.3	72.5±16.5	0.027
Median (range)	55.0 (20–90)	72.5 (40–100)	
PedsQL—Social	83.3±16.3	90.0±10.8	0.250
Median (range)	90.0 (45–100)	95.0 (60–100)	
PedsQL—School	66.6±16.3	75.9±14.0	0.026
Median (range)	70.0 (30–100)	77.5 (50–100)	
PedsQL—Psychosocial	68.3±13.5	79.4±10.3	0.001
Median (range)	69.3 (43.3-90)	80.8 (56.6-100)	

Continuous variables are expressed as the mean±SD and as the median with the minimum and maximum values in parenthesis

PedsQL^{TM}, Pediatric Quality of Life Inventory 4.0. There are four multidimensional subscales (physical functioning, emotional (psychological functioning, social functioning (5 items) and school functioning (5 items), and measures a total (global) scale (23 items) score and psychosocial (15 items) score

performance can be aggravated by school absenteeism. Delayed educational attainment was also described by Roscoe et al. [35] who reviewed medical records of 118 adolescents with CKD. These authors reported a delay in educational acquisition in all age groups and that 22 % of CKD adolescents did not finish high school. In a study which included adults with CKD since childhood, Morton et al. reported that 71 % of patients stated that they had interrupted their study due to illness [36]. In our study we also found marked differences in school attendance between controls and CKD patients, with 57 % of our patients reporting delayed educational acquisition—although this value is still within the average statistics for our country. The rate of age/grade inadequacy (percentage of children attending school who are not in their expected grades) in southeastern Brazil was between 37.4 and 68 % in 2000 according to a Brazilian census [37].

A previous history of psychiatric and/or psychological treatment may reflect a greater vulnerability to the development of psychiatric or behavioral disorders. In the study of Morton and colleagues, 47 % of CKD patients reported psychological problems during childhood, of whom 27 % had been referred for treatment [36]. In our sample, the frequency of previous referrals to a psychologist and/or a psychiatrist was 35.7 % among CKD patients, compared with only 3.5 % of controls. This finding was also associated with poorer overall HRQoL scores, and lower scores in the school, social and psychosocial subdomains.

Adjustment to chronic illness and the risk of behavioral morbidity is a complex and continuous process in which a variety of factors, other than disease-related parameters may influence psychosocial adjustment [11, 38]. Depression is one of the most studied psychiatric disorders and the most frequently in patients with ESRD [38, 39]. In our sample the average scores on the CDI did not differ between patients and controls. However, while the percentage of children and adolescents with CKD who exhibited clinically significant depressive symptoms was 14.3 %, none of the controls scored above this cut-off point in the CDI. Kogon et al. [14], also using the CDI, found a similar overall frequency (18 %) of clinically significant depressive symptoms in patients with CKD, with patients on dialysis being less likely than patients with pre-ESRD to be depressed. Using the Beck Depression Inventory to measure depression, Penkower and co-workers [40] identified a higher percentage (36.4 %) of significant depressive symptoms among adolescents 3 months after renal transplant.

The frequency of anxiety symptoms found in both CKD patients and controls is higher than that in the general population. However, the authors of the SCARED validation study in Brazil [33] found a prevalence of 37 % of at least one anxiety disorder, with mean scores of 23.51, which are similar to those scores of our controls (22.8). This elevated frequency might be explained by the screening nature of this highly

Table 4 Univariate analyses including gender, previous psychiatric treatment and depression in children and adolescents with chronic kidney disease

PedsQL™(global and subdomain scores) and resilience	Variable	Extract	CKD Patients			
			n	Median±SD	Standard error	*p*
PedsQL—Social	Sex	Female	10	92±13.8	4.4	0.027
		Male	18	80±16.1	3.8	
PedsQL—Global	Previous treatment	No	18	77.2±11.0	2.6	0.026
		Yes	10	65.7±14.6	4.6	
PedsQL—School	Previous treatment	No	18	72.5±11.4	2.7	0.008
		Yes	10	56.0±19.0	6.0	
PedsQL—Social	Previous treatment	No	18	88.9±14.9	3.5	0.018
		Yes	10	76.0±15.6	4.9	
PedsQL—Psychosocial	Previous treatment	No	18	73.5±12.5	3.0	0.005
		Yes	10	58.7±9.7	3.2	
Resilience	Depression	No	24	124.8±20.5	4.2	0.015
		Yes	4	86.5±26.9	13.4	

Variables are expressed as mean±SD and standard error

PedsQL™, Pediatric Quality of Life Inventory 4.0; CKD, chronic kidney disease

sensitive tool. Similar to our results, Kilis-Pstrusińska and colleagues [12] found no significant correlation between anxiety symptoms and clinical or laboratory parameters of CKD.

Fukunishi and colleagues [13] reported that 65.4 % of their a sample of 53 children and adolescents with CKD had separation anxiety. The percentage of our sample demonstrating this anxiety symptom, using the cut-off validated for the Brazilian population [33], was 22.7 %. While the average age in Fukunishi et al.'s study was 9.4 and 9.7 years for patients on peritoneal dialysis and post-transplant, respectively, the average age of our sample was 13.7 years. Separation anxiety affects around 5 % of children in the general population [41], but its frequency decreases as the children get older. Separation anxiety is associated with an increased risk of developing other psychiatric disorders, such as panic disorder [42]. Anxiety in children and adolescents with medical illnesses may develop in response to several factors. Pao and Bosk [43] proposed that anxiety could predispose biological mechanisms related to the disease itself as a response to being ill or in the hospital or as a result of genetic and other psychosocial factors. Also, parental anxiety can lead to interactions that are maladaptive in the long-term, determining separation difficulties, school phobia, body overconcern/dissatisfaction and school underachievement—a situation also referred to as the 'vulnerable child syndrome' [43, 44]. The 22 % frequency of separation anxiety found in our sample, composed mostly of teenagers, could be indicative of problems of children and adolescents with CKD in developing and acquiring autonomy [45].

Table 5 Psychiatric symptoms in chronic kidney disease patients and controls

SCARED and CDI instruments for psychiatric symptoms	CKD patients	Controls	*p*
SCARED—Global	28.0±14.3	22.8±7.7	0.094
Median (range)	25 (4–58)	22 (9–35)	
SCARED—Panic	5.7±5.1	4.0±3.8	0.351
Median (range)	4.0 (0–18)	3.0 (0–20)	
SCARED—General anxiety	8.2±4.0	7.6±2.8	0.616
Median (range)	9.0 (1–16)	8.0 (2–13)	
SCARED—Separation anxiety	6.5±3.3	4.5±1.9	0.018
Median (range)	7.0 (1–15)	5.0 (0–7)	
SCARED—Social anxiety	5.9±3.4	5.6±2.8	0.195
Median (range)	5.0 (0–13)	6.0 (1–12)	
SCARED—School anxiety	1.6±1.3	1.5±1.6	0.394
Median (range)	1.5 (0–5)	1.0 (0–8)	
CDI	9.8±6.8	6.9±3.2	0.092
Median (range)	8.0 (0–31)	7.0 (2–13)	
Significant anxiety symptoms (above cut-off score for SCARED)[a]	16 (57.1)	14 (50)	0.592
Significant depressive symptoms (above cut-off score for CDI)[b]	4 (14.3)	0	0.04

SCARED, Self-report for Childhood Anxiety Related Disorders; CDI, Child Depression Inventory; CKD, chronic kidney disease

Continuous variables are expressed as the mean±SD and as the median with the minimum and maximum values in parenthesis. Categorical variables are shown as number of cases with the percentage in parenthesis

[a] Cut-off point determined for the Brazilian population [33]

[b] Cut-off point determined for the Brazilian population [31]

In an attempt to investigate factors associated with psychiatric symptoms and impaired HRQoL, we included an evaluation of resilience in our study. Resilience has been conceptualized as a moderating factor between the burden associated with chronic diseases and the possibility of positive response to this burden [16]. In our study, resilience scores were similar in patients and controls, but lower scores were associated with depressive symptoms. This finding may indicate that children and adolescents with CKD may develop adaptive mechanisms to deal with the disease. Indeed, resilience does not equate to the suppression or avoidance of stress, but to the management of stressors in a positive manner, increasing self-confidence

and social competence [46]. Resilience was not associated with school attendance or with demographic and social parameters in our sample.

It is well established that multidisciplinary care improves the clinical outcomes (such as anemia management, bone mineral metabolism, nutrition) and renal disease progression in CKD pediatric patients [47]. The support of such a management team, which in our Pediatric Nephrology Unit consists of pediatric nephrologists, nurses, psychologists, nutritionists and social workers, may also have influenced the positive resilience scores among our patients, as previously described by Grunberg in a case study [6]. Resilience scores were lower among patients with clinically significant depressive symptoms, as has also been observed in previous studies [18, 48]. In addition, resilience scores were inversely correlated with depressive scores in the control group. Resilience, therefore, could be a protective factor against the development of psychiatric co-morbidity, especially depressive disorders. On the other hand, screening and identifying depression earlier could also favorably promote resilience [18]. An educational–behavioral intervention program (COPE), which included increasing parent information and participation in child care and activities (such as puppet play and stories about a young child who successfully copes with a stressful hospitalization), resulted in significantly fewer adjustment disorders in hospitalized children [49].

As with other chronic diseases and for adult patients with CKD, studies have identified impairment in HRQoL in children and adolescents with CKD [4, 6–9]. In our study, children and adolescents with pre-dialysis CKD achieved worse scores than controls in the global scores and in the psychological, educational and psychosocial subdomains. These findings are similar to those reported previously [4, 6–9].

More advanced stages of CKD were not associated with psychological variables, but we did study identify a correlation between patient age and disease duration and worse HRQoL scores. In addition, depressive symptoms negatively correlated with all (sub)domains of HRQoL, as observed in other studies [4, 50].

One of the major limitations of our study was the sample size, which was restricted by the age limits and by the inclusion of only pre-dialysis CKD patients. Another important limitation was the use of screening instruments of psychiatric symptoms and not structured clinical interviews for formal psychiatric diagnoses. Our evaluation included clinical and laboratory variables of CKD, but these patients may be under the influence of many other stressors that we were unaware of or unable to take into account. Future studies evaluating psychiatric morbidity and the HRQoL of caregivers could provide more information on these stressors. Longitudinal follow-up of these children and adolescents might clarify the role of resilience and psychiatric disorders on the progression of CKD. Although this was a cross-sectional study, it contributes to a broader understanding of pre-dialysis CKD pediatric patients since psychiatric morbidity, resilience and HRQoL were regarded as research priorities in the last report of the NIH Task Force [19].

In conclusion, the QoL of children and adolescents with pre-dialysis CKD was impaired compared to that of the controls, without any association with clinical or laboratory parameters. Patients and controls exhibited similar scores of resilience, but CKD negatively influenced HRQoL, contributing to a higher frequency of depression and separation anxiety in the pediatric CKD patients. More studies are needed in the pediatric population, especially those addressing factors associated with the promotion of resilience and the development of psychiatric symptoms or HRQoL impairment in CKD.

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References

1. Soares CM, Diniz JS, Lima EM, Silva JM, Oliveira GR, Canhestro MR, Colosimo EA, Simões e Silva AC, Oliveira EA (2008) Clinical outcome of children with chronic kidney disease in a pre-dialysis interdisciplinary program. Pediatr Nephrol 23:2039–2046
2. Nogueira PCK, Feltran LS, Camargo MF, Leão ER, Benninghoven JRCS, Gonçalves NZ, Pereira LA, Sesso RC (2011) Estimated prevalence of childhood end-stage renal disease in the state of São Paulo. Rev Assoc Med Bras 57:443–449
3. Harambat J, vanStralen KJ, Kim JJ, Tizard EJ (2012) Epidemiology of chronic kidney disease in children. Pediatr Nephrol 27:363–373
4. Marciano RC, Soares CM, Diniz JS, Lima EM, Silva JM, Canhestro MR, Gazzinelli A, Melo CC, Dias CS, Simões e Silva AC, Correa H, Oliveira EA (2011) Behavioral disorders and low quality of life in children and adolescents with chronic kidney disease. Pediatr Nephrol 26:281–290
5. McDonald SP, Craig JC, New Zealand Paediatric Nephrology Association (2004) Long-term survival of children with end-stage renal disease. N Eng J Med 350:2654–2662
6. Grünberg J, Verocay C, Rébori A, Amaral C (2005) The promotion of patient resilience in a pediatric dialysis unit: a case report. Humane Medicine [Internet]:5(2). Available at: http://www.humanehealthcare.com/Article.asp?art_id=816
7. Gerson AC, Riley A, Fivush BA, Pham N, Fiorenza J, Robertson J, Chandra M, Trachtman H, Weiss R, Furth SL, Council on Pediatric Nephrology and Urology of New York/New Jersey, Kidney and Urology Foundation of America (2005) Assessing health status and health care utilization in adolescents with chronic kidney disease. J Am Soc Nephrol 16:1427–1432
8. McKenna AM, Keating LE, Vigneux A, Stevens S, Williams A, Geary DF (2006) Quality of life in children with chronic kidney disease-patient and caregiver assessments. Nephrol Dial Transplant 21:1899–1905
9. Varni JW, Limbers CA, Burwinkle TM (2007) Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease

categories/severities utilizing the PedsQL 4.0 Generic Core Scales. Health Qual Life Outcomes 5:43
10. Pinquart M, Shen Y (2011) Depressive symptoms in children and adolescents with chronic physical illness: an updated meta-analysis. J Pediatr Psychol 36:375–384
11. Lavigne JV, Faier-Routman J (1992) Psychological adjustment to pediatric physical disorders: a meta-analytic review. J Pediatr Psychol 17:133–157
12. Kiliś-Pstrusińska K, Medyńska A, Adamczak P, Bałasz-Chmielewska I, Grenda R, Kluska-Jóźwiak A, Leszczyńska B, Olszak-Szot I, Miklaszewska M, Szczepańska M, Tkaczyk M, Wasilewska A, Zachwieja K, Zajączkowska M, Ziółkowska H, Zagożdżon I, Zwolińska D (2013) Anxiety in children and adolescents with chronic kidney disease—multicenter national study results. Kidney Blood Press Res 37:579–587
13. Fukunishi I, Kudo H (1995) Psychiatric problems of pediatric end-stage renal failure. Gen Hosp Psychiatry 17:32–36
14. Kogon AJ, Vander Stoep A, Weiss NS, Smith J, Flynn JT, McCauley E (2013) Depression and its associated factors in pediatric chronic kidney disease. Pediatr Nephrol 28:1855–1861
15. Masten AS, Best KM, Garmezy N (1990) Resilience and development: Contributions from the study of children who overcome adversity. Dev Psychopathol 2:425–444
16. Luthar SS, Cicchetti D, Becker B (2000) The construct of resilience: A critical evaluation and guidelines for future work. Child Dev 71:543–562
17. Ma LC, Chang HJ, Liu YM, Hsieh HL, Lo L, Lin MY, Lu KC (2013) The relationship between health-promoting behaviors and resilience in patients with chronic kidney disease. Sci World J 2013: 124973
18. Lee KY, Wang SM, Kim YR, Lee HK, Lee KU, Lee CT, Kweon YS (2012) The effect of resilience on depression and life satisfaction in patients with hemodialysis. J Korean Neuropsychiatr Assoc 51: 439–444
19. Chesney RW, Brewer E, Moxey-Mims M, Watkins S, Furth SL, Harmon WE, Fine RN, Portman RJ, Warady BA, Salusky IB, Langman CB, Gipson D, Scheidt P, Feldman H, Kaskel FJ, Siegel NJ (2006) Report of an NIH task force on research priorities in chronic kidney disease in children. Pediatr Nephrol 21:14–25
20. Hogg RJ, Furth S, Lemley KV, Portman R, Schwartz GJ, Coresh J, Balk E, Lau J, Levin A, Kausz AT, Eknoyan G, Levey AS, National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (2003) National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for chronic kidney disease in children and adolescents: evaluation, classification, and stratification. Pediatrics 111:1416–1421
21. Soares CM, Diniz JS, Lima EM, Oliveira GR, Canhestro MR, Colosimo EA (2009) Predictive factors of progression to chronic kidney disease stage 5 in a predialysis interdisciplinary program. Nephrol Dial Transplant 24:848–855
22. Schwartz GJ, Haycock GB, Edelmann CM Jr, Spitzer A (1976) A simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. Pediatrics 58:259–263
23. Langman CB, Salusky IB (2005) K/DOQI Clinical Practice Guidelines for bone metabolism and disease in children with chronic kidney disease—Foreword. Am J Kidney Dis 46:S6–S121
24. Levin A, Rocco MV (2006) KDOQI clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease—Foreword. Am J Kidney Dis 47:S9–S145
25. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (2004) The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 114:555–576
26. Wagnild GM, Young HM (1993) Development and psychometric evaluation of the Resilience Scale. J Nurs Meas 1:165–178
27. Pesce RP, Assis SG, Avanci JQ, Santos NC, Malaquias JV, Carvalhaes R (2005) Cross-cultural adaptation, reliability and validity of the resilience scale. Cad Saúde Pública 21:436–448
28. Varni JW, Seid M, Kurtin PS (2001) The PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. Med Care 39:800–812
29. Klatchoian DA, Len CA, Terreri RA, Silva M, Itamoto C, Ciconelli RM (2008) Quality of life of children and adolescents from São Paulo: reliability and validity of the Brazilian version of the Pediatric Quality of Life InventoryTM version 4.0 Generic Core Scales. J Pediatr 84:308–315
30. Kovacs M (1980) Rating scales to assess depression in school-aged children. Acta Paedopsychiatria 46:305–315
31. Golfeto JH, Veiga MH, Souza L, Barbeira C (2002) Psychometrical properties of the Inventory of Child Depression (CDI) in a sample of children in Ribeirão Preto. Rev Psiquiatr Clín 29:66–70
32. Birmaher B, Khetarpal S, Brent D, Cully M, Balach L, Kaufman J, Neer SM (1997) The Screen for Child Anxiety Related Emotional Disorders (SCARED): scale construction and psychometric characteristics. J Am Acad Child Adolesc Psychiatry 36:545–553
33. DeSousa DA, Salum GA, Isolan LR, Manfro GG (2013) Sensitivity and specificity of the Screen for Child Anxiety Related Emotional Disorders (SCARED): a community-based study. Child Psychiatry Hum Dev 44:391–399
34. Matta SM, Moreira JM, Kummer AM, Barbosa IG, Teixeira AL, Silva ACS (2014) Cognitive alterations in chronic kidney disease: an update. J Bras Nefrol 36:241–245
35. Roscoe JM, Smith LF, Williams EA, Stein M, Morton AR, Balfe JW, Arbus GS (1991) Medical and social outcome in adolescents with end-stage renal failure. Kidney Int 40:948–953
36. Morton MJS, Reynolds JM, Garralda ME, Postlethwaite RJ, Goh D (1994) Psychiatric adjustment in end-stage renal disease: A follow up study of former pediatric patients. J Psychosom Res 38:293–303
37. IBGE: Instituto Brasileiro de Geografia e Estatística [Internet]. Censo Demográfico 2000. Available at: http://www.ibge.gov.br/home/estatistica/populacao/censo2000/popu lacao/censo2000_populacao.pdf. Accessed Dec 2013
38. Cukor D, Coplan J, Brown C, Peterson RA, Kimmel PL (2008) Course of depression and anxiety diagnosis in patients treated with hemodialysis: a 16-month follow-up. Clin J Am Soc Nephrol 3: 1752–1758
39. Moreira JM, Matta SM, Kummer AM, Barbosa IG, Teixeira AL, Silva ACS (2014) Neuropsychiatric disorders and renal diseases: an update. J Bras Nefrol 36:396–400
40. Penkower L, Dew MA, Ellis D, Sereika SM, Kitutu JM, Shapiro R (2003) Psychological distress and adherence to the medical regimen among adolescent renal transplant recipients. Am J Transplant 3: 1418–1425
41. Masi G, Mucci M, Millepiedi S (2001) Separation anxiety disorder in children and adolescents: epidemiology, diagnosis and management. CNS Drugs 15:93–104
42. Brückl TM, Wittchen HU, Höfler M, Pfister H, Schneider S, Lieb R (2007) Childhood separation anxiety and the risk of subsequent psychopathology: Results from a community study. Psychother Psychosom 76:47–56
43. Pao M, Bosk A (2011) Anxiety in medically ill children/adolescents. Depress Anxiety 28:40–49
44. Forsyth BW, Horwitz SM, Leventhal JM, Burger J, Leaf PJ (1996) The child vulnerability scale: an instrument to measure parental perceptions of child vulnerability. J Pediatr Psychol 21:89–101
45. Castro EK, Piccinini CA (2002) Implications of physical chronic disease in childhood to family relationships: some theoretical questions. Psicol Refl Crít 15:625–635

46. Rutter M (1985) Resilience in the face of adversity. Protective factors and resistance to psychiatric disorder. Br J Psychiatry 147:598–611
47. Ajarmeh S, Er L, Brin G, Djurdjev O, Dionne JM (2012) The effect of a multidisciplinary care clinic on the outcomes in pediatric chronic kidney disease. Pediatr Nephrol 27:1921–1927
48. Hjemdal O, Aune T, Reinfjell T, Stiles TC, Friborg O (2007) Resilience as a predictor of depressive symptoms: a correlational study with young adolescents. Clin Child Psychol Psychiatry 12: 91–104
49. Melnyk BM, Alpert-Gillis L, Feinstein NF, Crean HF, Johnson J, Fairbanks E, Small L, Rubenstein J, Slota M, Corbo-Richert B (2004) Creating opportunities for parent empowerment: program effects on the mental health/coping outcomes of critically ill young children and their mothers. Pediatrics 113:597–607
50. Santos JB, Mendonça M, Pinheiro MC, Tamai S, Uchida R, Miorin LA, Sanches M (2010) Negative correlations between anxiety-depressive symptoms and quality of life among patients on hemodialysis. Sao Paulo Med J 128:102–103