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Original Article

Impact of end-stage renal disease on psychological status and quality of life

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Abstract ***Background*:** The aim of this study was to assess depression, anxiety, and quality of life (QOL) in a cohort of children and adolescents with end-stage renal disease (ESRD), to compare these findings with healthy controls, and to evaluate the association between these psychological symptoms, QOL, and clinical variables related to ESRD.

***Methods*:** Thirty-two children and adolescents 8–18 years of age were enrolled in the study. The sociodemographic data were evaluated. Questionnaires were used to evaluate the psychological status and QOL of the patients and healthy controls.

***Results*:** There was a significant difference in mean depression score, which was significantly higher for the ESRD patients. Mean state anxiety score was significantly lower for ESRD patients than for controls. Regarding QOL score, there were significant differences between the ESRD patients and control groups for both child-rated and parent-rated QOL scores, which were significantly lower for ESRD patients. Trait anxiety was a negative predictor of all subscales of the Pediatric Quality of Life Inventory 4.

***Conclusions*:** End-stage renal disease was related to significant morbidity and poorer QOL. The assessment and enhancement of QOL and comorbid psychiatric disorders in ESRD should be a part of disease management.

Key words adolescent, child, end-stage renal disease, psychological symptom, quality of life.

Mortality and morbidity rates of end-stage renal disease (ESRD), both in adults and children, tend to decrease in parallel with recent advances in medicine.[1–3] In spite of all these advances, the chronic and progressive nature of renal failure and the complexity of ESRD leads to physiological, psychological, and social problems and lowers quality of life (QOL).[4–7] Studies of adults with ESRD have reported higher levels of psychological symptoms and lower QOL.[8–11] Psychiatric disorders, particularly depressive disorders, may increase the mortality and morbidity rates in adults with ESRD.[11–13]

To our knowledge, many studies have examined psychological factors and ESRD, but only a few studies have explored the association between psychological status, clinical characteristics, and QOL in children and adolescents with ESRD. The objectives of this study were therefore (i) to assess depression, anxiety, and QOL in a cohort of children and adolescents with ESRD and to compare these findings with healthy controls; and (ii) to evaluate the association between these psychological symptoms, QOL, and clinical variables related to ESRD. The hypothesis was that patients with ESRD would have higher depression and anxiety, but lower QOL than healthy controls and their parents. It was also hypothesized that the elevated depressive and anxiety symptoms would be associated with significantly worse QOL in the ESRD patient group.

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Methods

This case–control study was conducted from February to August 2014 in the Department of Pediatric Nephrology of Istanbul University Cerrahpasa Medical Faculty Hospital in Turkey. Forty-three patients asked to be enrolled the study. Three patients or their parents failed to fill out the forms, and seven patients or their parents did not complete the scales properly. One patient's parent was illiterate. The participants consisted of 32 children and adolescents aged 8–18 years and who were followed up on chronic dialysis programs (hemodialysis [HD] or peritoneal dialysis [PD]) or as transplant recipients and their primary caregivers. The main underlying causes of ESRD were congenital anomalies of the kidney and urinary tract (CAKUT) with/without obstruction in 11 patients, glomerular disease in five, neurogenic bladder in five, cystinosis in four, oxalosis, hemolytic uremic syndrome and autosomal recessive polycystic kidney disease in one patient each,

and unknown origin in four patients. The inclusion criteria were as follows: age 8–18 years; chronic renal insufficiency (CRI), defined as plasma creatinine >20 mmol/L; and ESRD requiring maintenance dialysis or renal transplantation. Patients were excluded if they or their caregivers were illiterate or handicapped or failed to fill out the forms. All eligible participants were informed about the study procedures, and only those who volunteered were enrolled in the study. The mean time for completing the scales was approximately 20 min for both the patient and the caregiver. The study protocol was reviewed and approved by the ethics committee of Bakirkoy Research and Training Hospital for Psychiatry, Neurology, and Neurosurgery. It complied with the 1964 Helsinki declaration and its later amendments or comparable ethics standards. The control group consisted of 45 healthy children from the local community who were eligible and matched for gender, age, and parent education level. All participants enrolled in the study gave informed consent.

Demographic and clinical variables

A standardized form was used to collect demographic (age, gender, race, and educational status) and clinical data. Clinical data included hemoglobin, height *z*-scores, etiology of ESRD, age at onset of the illness, and duration of the illness.

Psychological measures

The Pediatric Quality of Life Inventory Parent Version (PedsQL-P) and the Pediatric Quality of Life Inventory Child Version (PedsQL-C), developed to evaluate child QOL, were completed by caregivers and ESRD patients, respectively.[14] While these scales are not specific to renal disease, they have been used in children with many different diseases. They contain two subscale scores: psychosocial and physical health; and a total score. The scale contains both parent and child versions for physical and psychosocial functioning; a higher PedsQL total score indicates better QOL. In this study, PedsQL-P was administered to parents. If the parent was unavailable to complete the questionnaires, other caregivers were asked to do so. We used the validated Turkish versions of these questionnaires in this study, and the internal consistency of the child self-report was determined as 0.86 and that of the parent proxy report as 0.88.[15,16] We used a generic scale for QOL because there was no specific scale for ESRD patients translated to Turkish.

The Child Depression Inventory (CDI), a self-report depression scale for children between 6 and 18 years old, was used to measure depressive symptoms for the previous 2 weeks.[17] The reliability study of the Turkish version was conducted by Öy, and the reliability of the scale (Cronbach's alpha) was 0.76.[18] Higher scores indicate greater severity of depression. The cut-off point of the CDI in the Turkish version was 19.

The State–Trait Anxiety Inventories for Children (STAI-C) is a Likert-type scale with two subscales: state and trait anxiety.[19] State anxiety is anxiety experienced under certain conditions, at a certain time, and is affected by alterations in external factors. In contrast, trait anxiety refers to the general feelings of an individual and reflects the individual's general predisposition to anxiety. The inventories were adapted to Turkish by Özusta, and Cronbach's alpha for the scales was 0.81.[20] Higher scores indicate greater severity of anxiety.

The mean scores of depression, state and trait anxiety, and QOL were evaluated across the ESRD patient and control groups.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (SPSS, Chicago, IL, USA). The chi-squared test was used, as appropriate, to analyze differences between groups in categorical variables. Mann–Whitney *U*-test was used to analyze differences in continuous variables between the dialysis and transplant groups. For the three-group comparison of continuous variables, Kruskal–Wallis test was used; if significant, follow-up pairwise comparison was then carried out. Because of the risk of type I error due to multiple testing effect, adjusted *P*-values were taking into account for follow-up pairwise comparison. The Pearson or the Spearman correlation coefficient was calculated to examine the relationship between the psychological test scores. Multivariate linear regression analysis was conducted to assess the determinants of QOL score. Two-tailed $P < 0.05$ was considered statistically significant.

Results

Thirty-two ESRD patients (all Caucasian) who met the eligibility requirements participated in this study. Mean age of the transplant group was 13.8 ± 2.3 years, and that of the dialysis group, 14.3 ± 2.1 years (range, 8–18 years); together these two groups consisted of 13 male patients (40.6%) and 19 female patients (59.4%). Mean renal replacement therapy duration was 5.56 ± 3.71 years. No significant differences were found between the ESRD patients and controls in terms of age, gender, and parental education. Of the ESRD patients, 13 (40.6%) were transplant recipients, 11 (34.4%) were receiving PD, and eight (25.0%) were on HD (Table 1).

Mean depression, state and trait anxiety, and QOL scores of the ESRD patient (transplant and dialysis) and control groups are listed in Table 2. Nine ESRD patient CDI scores were >19. There was a significant difference in mean depression score, which was significantly higher in the dialysis group. Mean state anxiety score, however, was significantly lower for the transplant patients compared with the control and dialysis groups. Regarding QOL score, there were significant differences between the dialysis and control groups for both child-rated scores, which were significantly lower for the dialysis patients; but for the parent proxy reports only physical health score was not significantly different from the control group. With regard to psychosocial and total scores, these were both significantly lower in the transplant and dialysis patients compared with the control group (Table 2).

Table 1 Clinical and demographic features

Demographic variables	Transplant (n = 13)	Dialysis (n = 19)	Controls (n = 45)	$H/z/\chi^2$	*P*-value
Age (years)	13.8 ± 2.3	14.3 ± 2.1	13.6 ± 2.4	0.97†	0.616
M/F	7/6	6/13	21/24	1.83‡	0.401
Hemoglobin (g/dL)	11.6 ± 1.8	10.4 ± 1.9	—	1.69§	0.091
Age of onset of CRF	4.8 ± 5.3	5.5 ± 4.9	—	0.51§	0.608
Duration of illness (months)	9.0 ± 4.6	8.7 ± 5.1	—	0.27§	0.788
Father's educational level (years)	7.7 ± 3.4	7.3 ± 3.6	7.6 ± 3.8	0.32†	0.853
Mother's educational level (years)	5.1 ± 3.4	4.7 ± 3.3	6.1 ± 2.6	4.54†	0.103

†Kruskal–Wallis test; ‡Mann–Whitney *U*-test; §Chi squared test. CRF, chronic renal failure.

Table 2 Mean depression, state and trait anxiety, and QOL scores

	A. Transplant (n = 13)	B. Dialysis (n = 19)	C. Controls (n = 45)	Kruskal–Wallis test	Adjusted *P* (A vs B)	Adjusted *P* (A vs C)	Adjusted *P* (B vs C)
CDI	12.2 ± 7.3	14.2 ± 7.6	8.9 ± 6.2	H (2) = 7.79, P = 0.020	NS	NS	0.041
STAI-C							
State-anxiety	30.8 ± 7.4	33.9 ± 7.0	38.9 ± 8.9	H (2) = 10.51, P = 0.005	NS	0.018	NS
Trait-anxiety	35.6 ± 7.7	36.5 ± 8.5	34.7 ± 5.6	H (2) = 0.35, P = 0.841	NS	NS	NS
PedsQL-C							
Physical health	69.5 ± 13.7	54.8 ± 20.7	78.7 ± 14.3	H (2) = 20.23, P < 0.001	NS	NS	<0.001
Psychosocial	69.4 ± 14.1	58.9 ± 20.2	78.2 ± 9.9	H (2) = 17.66, P < 0.001	NS	NS	<0.001
Total	69.4 ± 12.1	57.5 ± 18.5	78.4 ± 9.2	H (2) = 24.74, P < 0.001	NS	NS	<0.001
PedsQL-P							
Physical health	57.2 ± 17.7	58.2 ± 25.9	70.9 ± 18.9	H (2) = 6.45, P = 0.040	NS	NS	NS
Psychosocial	60.9 ± 16.7	52.5 ± 16.9	77.1 ± 11.1	H (2) = 28.15, P < 0.001	NS	0.014	<0.001
Total	59.6 ± 15.0	54.5 ± 16.2	74.9 ± 11.7	H (2) = 23.77, P < 0.001	NS	0.012	<0.001

CDI, child depression inventory; PedsQL-C, Pediatric Quality of Life Inventory Child Version; PedsQL-P, Pediatric Quality of Life Inventory Parent Version; QOL, quality of life; STAI-C, State–Trait Anxiety Inventories for Children.

Table 3 Correlations between QOL, psychological test scores and clinical variables

	CDI	Trait anxiety	State anxiety	Duration of illness	Age at onset of illness	Hemoglobin	Height (*z*-scores)
PedsQL-C physical health	−0.36*	−0.53***	−0.35	0.15	−0.25	0.37*	0.44*
PedsQL-C psychosocial	−0.74***	−0.71***	−0.51**	0.04	−0.10	0.16	0.40*
PedsQL-C total	−0.67***	−0.71***	−0.50**	0.08	−0.17	0.26	0.45**
PedsQL-P Physical Health	0.04	0.08	−0.31	0.17	−0.09	0.23	−0.16
PedsQL-P psychosocial	−0.58**	−0.41*	−0.64***	0.03	−0.12	0.14	0.01
PedsQL-P total	−0.39*	−0.25	−0.61***	0.11	−0.13	0.21	−0.08

*P < 0.05; **P < 0.01; ***P < 0.001. CDI, child depression inventory; PedsQL-C, Pediatric Quality of Life Inventory Child Version; PedsQL-P, Pediatric Quality of Life Inventory Parent Version; QOL, quality of life; STAI-C, State–Trait Anxiety Inventories for Children.

Correlations between clinical variables, such as age of onset, duration of illness, hemoglobin, height *Z*-score, and severity of depression and anxiety, were evaluated for the ESRD patient group. There was no significant association between clinical variables and depression and anxiety scores. The correlation of psychiatric questionnaires scores and clinical variables with QOL score was also assessed. The CDI, State Anxiety Inventory (SAI), and Trait Anxiety Inventory (TAI) scores were generally negatively correlated with the subscale scores of the PedsQL-C and P, except the PedsQL-P physical health score, indicating that a higher level of depressive and anxiety symptoms was associated with poorer QOL. Height *Z*-score was positively correlated with all PedsQL-C subscale scores. Hemoglobin was positively correlated with only the PedsQL-C physical health subscale score (Table 3).

According to regression analysis, trait anxiety was a negative predictor of all PedsQL-C subscales, and depression was a negative predictor of the PedsQL-C psychosocial subscale (Table 4). In addition, state anxiety was a negative predictor of both the PedsQL-P psychosocial subscale and PedsQL-P total scores (Table 5).

Discussion

The present study has shown that ESRD is related to greater severity of depressive symptoms (and that this is more

Table 4 Multivariate predictors of child-rated QOL in pediatric ESRD

	B	SE B	β	*t*	*P*	R^2
PedsQL-C physical health						0.367
Trait anxiety	−1.10	0.50	−0.46	−2.20	0.036	
CDI	0.08	0.54	0.03	0.14	0.888	
Height (Z score)	2.08	1.05	0.31	1.99	0.056	
PedsQL-C psychosocial						0.656
Trait anxiety	−0.80	0.36	−0.35	−2.25	0.033	
State anxiety	0.01	0.42	0.01	0.03	0.975	
CDI	−1.14	0.48	−0.46	−2.37	0.025	
Height (Z score)	1.13	0.75	0.18	1.51	0.143	
PedsQL-C total						0.626
Trait anxiety	−0.90	0.34	−0.43	−2.64	0.014	
State anxiety	−0.20	0.40	−0.08	−0.49	0.626	
CDI	−0.57	0.47	−0.25	−1.24	0.227	

CDI, child depression inventory; ESRD, end-stage renal disease; PedsQL-C, Pediatric Quality of Life Inventory Child Version; QOL, quality of life.

Table 5 Multivariate predictors of parent-rated QOL in pediatric ESRD

	B	SE B	β	*t*	*P*	R^2
PedsQL-P psychosocial						0.436
State anxiety	−1.07	0.47	−0.45	−2.27	0.031	
CDI	−0.59	0.46	−0.26	−1.30	0.204	
PedsQL-P total						0.369
State anxiety	−1.44	0.46	−0.66	−3.14	0.004	
CDI	0.16	0.44	0.08	0.36	0.719	

CDI, child depression inventory; ESRD, end-stage renal disease; PedsQL-P, Pediatric Quality of Life Inventory Parent Version; QOL, quality of life.

significant in dialysis patients), but to lower state anxiety in transplant patients compared with the dialysis and control groups in childhood and adolescence. This study also provided evidence relating ESRD to poor QOL, especially in dialysis patients compared with transplant recipients and healthy controls in this age group. Furthermore, trait anxiety and depressive symptoms were negative predictors of QOL in the ESRD subjects.

To date, there has been a limited number of studies on the psychological aspects of children with ESRD.[21–23] The present findings indicate greater severity of depressive symptoms in children with ESRD, especially in the dialysis patients than the control group. Amr *et al.* reported a significantly higher level of depressive symptoms on the depression scale of the Child Behavior Checklist in dialyzed children than in healthy children,[24] consistent with the present findings. In the USA, depression was the most common comorbid psychiatric disorder in adult patients with ESRD.[25] Although information on the relationship between ESRD and depression in children and adolescents is limited, existing data were consistent with adult studies. Kogon *et al.* found a 30% prevalence rate of depression in children and adolescents with ESRD.[26]

Adult studies have tended to reported higher scores for anxiety symptoms in patients with ESRD.[27–29] Little information is available, however, on the association between anxiety and ESRD in childhood.[24,30] Kiliś-Pstrusińska *et al.* found no significant difference in the anxiety level of ESRD and healthy controls, except for HD patients. In the HD group, children between 8 and 12 years of age had a higher level of state anxiety, but adolescents with HD had both higher state anxiety and trait anxiety.[31] We found no significant difference in trait anxiety between transplant–dialysis patients and the control group, which may be a result of partial adaptation to ESRD. We also noted significantly higher state anxiety in the control group than the transplant recipient group. Although we cannot explain the unexpected higher state anxiety in the control group, it is possible that the greater active coping strategy of fighting spirit, self-efficacy (coping capacity), and social support in pediatric transplant recipients may be associated with lower state anxiety.[32]

Lower QOL score is associated with increased morbidity and mortality in adult patients with ESRD.[33,34] In addition, the QOL of children with ESRD has been found to be significantly lower than in healthy control groups.[3,4,35] In the present study, dialysis patients and their parents reported significantly worse QOL in all PedsQL subscales. Parent perception of child QOL was worse than the children's perception, which is consistent with a previous study.[36] For the transplant recipients, there was no significant difference in QOL compared with the control group. This may be the result of the positive effects of transplantation. Prior studies have also reported that children with other chronic diseases, such as acute lymphoblastic leukemia and diseases leading to liver transplantation, had a better QOL than children with ESRD.[35,37] The present study indicates a marked burden of ESRD on the QOL of children and adolescents, and these results seem to be consistent with previous reports.

In the present study, depression, state and trait anxiety, and short stature were significant factors associated with worse QOL in pediatric ESRD patients. In proxy reports, the PedsQL psychosocial subdomain was negatively associated with depression and state and trait anxiety scores in ESRD patients. Although anxiety level was not higher than that in the healthy control group, SAI and TAI scores were negatively correlated with QOL. No relationship, however, was seen between QOL and the other clinical variables, including duration of illness and age of onset. Only hemoglobin was positively correlated with ESRD patient physical health scores. To our knowledge, there have been few studies on children and adolescents with ESRD regarding the effect of clinical variables on psychosocial wellbeing.[38] Data and knowledge on the relationship between clinical variables and QOL in ESRD relies considerably on adult studies. In adult studies, depression and anxiety have been negatively correlated with QOL.[1,32,39–42] Studies with children have noted a positive correlation between QOL and duration of illness and age, but a negative correlation between short stature and QOL.[35,43,44] The present results are similar to the aforementioned adult research findings, in that

clinical, functional, and psychological variables were significantly related to physical health, psychosocial, and total QOL scores.

We also investigated the distribution of possible clinical and psychological determinants of QOL, and the association between these determinants and QOL in the ESRD patient group on multivariate linear regression analysis. Trait anxiety predicted negative effects on all domains of the PedsQL-C, and CDI was also a negative predictor of the PedsQL-C psychosocial subscale. In the PedsQL parent proxy reports, children's state anxiety was a negative predictor of psychosocial and total subscales. In adult studies, anxiety and depression were the main predictors of poor QOL.[1,32] To our knowledge, no study has investigated the psychological predictors of QOL in children and adolescents with ESRD. There has been research, however, on clinical variables, such as short stature, anemia, gender, age at study entry, level of maternal education, and QOL. While Gerson *et al.* reported no clinical predictors of QOL in mild–moderate CRI, Al-Uzri *et al.* noted a significant association between catch-up growth and physical and social functioning. This inconsistency with regard to clinical variables in the pediatric literature may have resulted from the differences in etiology, clinical course, comorbidity, and treatment modalities of the diseases.[38,43] According to the present study depressive symptoms and trait anxiety were the most important predictors of QOL in pediatric ESRD, which is consistent with the adult studies on patients with ESRD.[1,32]

The present study has several limitations that should be taken into consideration when interpreting the results. First, the sample size was relatively small, and as a result the HD, PD, and transplant patients could not be assessed as separate groups, which may be a limiting factor for the generalization of the results. Moreover, sample size is important to establish an acceptable model for multivariate regression analyses; the present small sample size also prevented identification of the determinants of QOL in the HD, PD, and transplant patients separately. Second, a structured psychiatric interview was not performed for the ESRD patient and control groups, which could have prevented the gaining of a broader view of psychological status and psychiatric disorders. Another important limitation of the study was the absence of a QOL questionnaire specific for children with ESRD in Turkish. For this reason, a disease-specific questionnaire could not be used to measure QOL, which may restrict the valid and reliable determination of QOL. The present study was conducted in a single center, however, and therefore all patients were treated by the same clinical team, which is a strength of the study.

In conclusion, ESRD is related to significant morbidity and poorer QOL. The present study shows that ESRD is related to poorer QOL in childhood, but, after kidney transplantation, it has positive effects on QOL in pediatric ESRD patients and also on anxiety and depression. On multivariate regression analysis, psychological factors in particular are determinants of impaired QOL. The assessment and enhancement of QOL and comorbid psychiatric disorders in ESRD should be included in the disease management. Clinics should include measures of QOL in addition to measures of psychological symptoms for children in clinical practice. Moreover, there is a need for mental health workers in the care centers so that these patients and their families can improve their adjustment and coping strategies. Further prospective studies to better clarify the relationship between ESRD and psychological status and QOL in children and adolescents, as well as in pediatric HD, PD, and transplant patients, are warranted.

Disclosure

The authors declare no conflicts of interest.

Author contributions

A.G.K. was responsible for the study planning, conception, design, revision of all drafts of the manuscript, data collection, literature review, and English-language editing. K.B. was responsible for the study planning, conception, design, revision of all drafts of the manuscript, data analysis, and literature review. N.C. was responsible for the study conception, design, revision of all drafts of the manuscript, and data collection. A.B. was responsible for the study conception, design, revision of all drafts of the manuscript, data analysis, and English-language editing. C.M. was responsible for the study conception, design, revision of all drafts of the manuscript, and literature review. O.Y. was responsible for the study conception, design, revision of all drafts of the manuscript, and English-language editing. G.P. was responsible for the study conception, design, revision of all drafts of the manuscript, and data collection. L.S. was responsible for the study conception, design, revision of all drafts of the manuscript, and data collection. All authors read and approved the final manuscript.

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