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Review:

Role of Health-related Quality of Life Assessment in Children with Chronic Kidney Disease.

Samuel N Uwaezuoke and Vivian U Muoneke

Paediatric Nephrology Firm, Department of Paediatrics, University of Nigeria Teaching Hospital, Ituku-Ozalla Enugu, Nigeria

Abstract

This review aims to highlight the increasing importance of Health-related Quality of Life assessment in the management of children with early and late stages of chronic kidney disease. The growing interest in using Health-related Quality of Life assessment is attributed to the more active role of the patients and their expressed interest in the nonclinical aspects of treatment such as Quality of Life. Several measures of Health-related Quality of Life are now used in research and clinical practice to evaluate treatment options and make therapeutic decisions. Despite the technological advances in renal replacement therapy which have resulted in increased survival rates for children with Stage 5 chronic kidney disease (end-stage renal disease), the burden and complexity of care impacts negatively on their Quality of Life. Studies reviewed in this article show that children with end-stage renal disease receiving renal replacement therapy, as well as those with early stages of chronic kidney disease had significantly lower Health-related Quality of Life scores when compared with healthy controls. As a therapeutic guide to the clinician, appropriate and timely interventions may result in better Quality of Life outcomes in the fundamental domains. Although Health-related Quality of Life assessment is seen as a reliable adjunct in managing children with chronic kidney disease, the major challenge remains convincing more clinicians to apply this assessment beyond clinical trials as many of them still depend on physiologic measures in the clinical setting.

Keywords: Health-related quality of life, Chronic kidney disease, Children, Adjunct, Patient management

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Introduction

The current definition of chronic kidney disease (CKD) in children, according to the guidelines of the Kidney Disease Outcomes Quality Initiatives (K/DOQI), is based on the presence or absence of markers of kidney damage and the level of glomerular filtration rate (GFR) irrespective of the type of kidney damage [1]. Five stages of CKD are now recognized depending on the degree of impairment of glomerular filtration.

Medical and surgical advances have resulted in dramatic changes in physical outcomes and increases in survival rates for children with stage 5 CKD or end-stage renal disease (ESRD) [2]. Improvements in renal replacement therapy (RRT) have ensured their survival into adulthood [3]. However, the optimal care for the paediatric patient with CKD should also involve the management of psychosocial and developmental factors which will engender a successful transition into adult life [4]. Thus, the quality of survival is seen as equally important and has become a fundamental focus of comprehensive health care [5].

The goal of every health care is to make the patient feel better. Patient-reported outcome (PRO) measures can play a vital role in assessing whether this feeling of well-being has been achieved in routine clinical care. Some authors have documented that self-assessed health status has proved to be a more powerful predictor of mortality and morbidity than many objective measures of health [6, 7]. There is increasing evidence that patient-reported outcomes (PROs) - most importantly Health-related Quality of Life (HRQOL) - are more reliable indicators of the positive and negative impact
of disease and treatment than clinical opinion. Previously published studies have also shown that many children with advanced kidney disease have significant HRQOL impairments [8-11]. Thus, utilisation of HRQOL scores can help to improve patient management and Quality of Life outcomes since these measures can signal the need for

supportive interventions, serve as prognostic indicators and aid the clinician's decisions on therapeutic options.

This review aims to highlight the increasing importance of HRQOL assessment as a reliable adjunct in the management of paediatric CKD.

Definition of Health-related Quality of Life (HRQOL)

Several definitions of HRQOL have been proposed [12-15] but the consensus definition is that HRQOL refers to the functional effect of a medical condition and/or its consequent therapy upon a patient [15]. It is a multidimensional concept which encompasses domains related to physical and occupational function, psychological/ emotional state, social interaction and somatic sensation [16]. HRQOL should be patient-reported and should not be judged by a healthcare professional.

The goal of HRQOL assessment is to quantify the degree to which the medical condition or its treatment impacts on the individual's life in a valid and reproducible way. Along with traditional physiologic measures, it is an important indicator to capture the burden of disease. Although the gold standard is for patients to self-report their HRQOL, there may be room for proxy data especially when the patient is too ill or too young. These measurements can then be utilized to assess changes in HRQOL over time especially in clinical trials and healthcare delivery settings, and to compare the HRQOL of patients with different medical conditions or patients who receive different treatment modalities [13]. For instance, in paediatric ESRD, HRQOL is an important clinical measure of the effects of the disease, as well as the beneficial effects of management for children undergoing treatment modalities like haemodialysis (HD), peritoneal dialysis (PD) and renal transplantation (TX).

Health-related Quality of Life instruments: uses and draw-backs

Many generic and disease-specific HRQOL instruments are currently in use. The generics include SF-36 (a multipurpose short-form health survey composed of 36 questions which provide an eight-scale profile of functional health and well-being scores) [17], the Sickness Impact Profile (SIP) [18], and the EuroQol [19].

For healthy children, children with kidney disease and other chronic medical conditions, the Pediatric Inventory of Quality of Life Core Scales (PedsQL) 4.0- a generic HRQOL instrument that assesses physical, emotional, social, and school functioning in children and adolescents- has been reported as an appropriate measurement instrument [20, 21]. Currently, no ESRD-specific instrument for children has been established although Goldstein et al has recently developed a Ped QL 3.0 ESRD module which requires additional validation tests [22]. On the other hand, disease-specific instruments of HRQOL are increasingly being used to evaluate medical therapies [23], to make therapeutic decisions [24] and to allocate resources [25].

Despite the benefits of these PROs in patient care, the barriers to using them in a clinical setting include their time-consuming nature, poor questionnaire design, doctors' perception that their experience is sufficient enough to assess QOL, inability to score and analyze data, as well as difficulties in interpreting data [26].

Modalities of Renal Replacement Therapy and treatment-related issues

The preferred renal replacement therapy (RRT) for all patients with stage 5 CKD (ESRD) is successful kidney transplantation. However, nearly 75% of children with ESRD must be on maintenance dialysis for a month or one year to several years as they wait for a transplant [27, 28].

Broadly, RRT can be classified as intermittent or continuous, based on treatment duration. Intermittent therapies (less than 24 hours) include intermittent hemodialysis (IHD) and sustained low-efficiency dialysis (SLED) while the continuous therapies (at least 24 hours) consist of peritoneal dialysis (PD) and continuous RRT (CRRT).

Amongst these modalities, PD is the preferred initial RRT for children [28]. Although the majority of children who have stage 5 CKD (ESRD) requiring dialysis can be managed with maintenance PD, a multi-centre report in Europe indicates that the choice of dialysis modality is generally based on the preference of the patient and family, the philosophy of the centre and availability of the desired modality [29].

With respect to RRT in children and adolescents, the burden and complexity of care are enormous. The burden of care entails the time and attention required by the patients and their families which includes, for instance the number of medications patients take once to several times per day with dialysis and kidney transplant patients requiring the largest number (particularly the first 6-12 months post-transplantation) [30]. The complexity of care involves procedures such as self-catheterization, fluid and dietary restrictions, daily blood pressure measurements and so forth.

Obviously, the time-consuming nature and invasiveness of RRT place high demands on children and their families with restriction of physical and social activities [31].
Furthermore, children and adolescents on long-term dialysis are reported to be at greater risk for problems with psychological adjustment [31]. Worse still, they have difficulty adjusting to the diagnosis of ESRD and to subsequent dialysis- resulting in non-compliance to therapy.

One study has identified older age (adolescence), low family socio-economic status, duration of dialysis and living in a single-parent home as factors associated with reduced adherence to dialysis [32].

For children who require dialysis, the stage of CKD has been shown to affect neuro-cognitive development. Another study has demonstrated that patients with earlier stages of CKD had better cognitive performance scores compared with their counterparts receiving maintenance dialysis [33]. The neurocognitive issues associated with CKD appear to put children at risk for long-term sequels as the problems of these patients with neurocognitive delays seem to persist into adulthood [34]. Apart from these, patients also experience other treatment-related issues such as anuria, recurrent peritonitis, hernia and continuous glucose absorption depending on the modality of dialysis [28]. Successful renal transplantation (TX) provides the best outcome measure for children who initiate dialysis therapy. However, a long transplant list, social factors and disease-related morbidity may require long-term dialysis. Several factors have been identified to influence outcome for those who will require prolonged dialysis namely age of commencing dialysis, duration and modality of dialysis, co-morbid conditions and the cause of primary disease that resulted in ESRD, as well as treatment-related factors such as vascular access, dialysis adequacy, residual kidney function, nutrition and growth [2, 35].

Health-related Quality of Life assessment: its clinical application in paediatric CKD

HRQOL assessment is beneficial to patients, clinicians, researchers, health administrators and policy makers. Thus, medical research has focused increasingly on HRQOL as an important variable [36]. A key distinguishing feature of QOL is the incorporation of the patient's values, judgments and preferences [37]. An international group of investigators have suggested six fundamental domains of HRQOL: physical functioning, psychological functioning, social functioning, role activities, overall life satisfaction and perception of health status [38]. Some authors argue that each domain of health can be measured in objective and subjective dimensions [39]. The objective dimension serves to define a patient's degree of health while the patient's subjective evaluation serves to translate that health status into the actual QOL experienced [36]. From the patient's perspective, a meaningful change in HRQOL may be one that results in a meaningful reduction in symptoms or improvement in function while a meaningful change for the clinician may be one that indicates a change in the therapeutic option or in the prognosis of the disease [36].

Early identification of HRQOL problems in children with early stages of CKD and appropriate intervention may decrease the prevalence of poor educational, occupational and social outcomes in adults with childhood onset of CKD [40].

In fact, the importance of evaluating the behavioral and social repercussions in children with CKD in order to improve their QOL was buttressed in a study by a group of collaborative researchers [41]. Using Strengths and Difficulties Questionnaire (SDQ) and Pediatric Inventory of Quality of Life Core Scales (PedsQL) as assessment tools for patients and care-givers, the prevalence of behavior disorders and assessment of HRQOL in 136 patients with CKD was done. When compared to healthy controls, the CKD group had significantly lower scores in almost all PedsQL domains [41]. This finding supports the argument that unless assessments of HRQOL come directly from the patient, investigators are not measuring HRQOL [37]. Other researchers have observed that children can perceive their QOL as good, despite living with what others may perceive as severe limitations [42].

Furthermore, other studies have reported lower scores on HRQOL assessment and greater psychosocial impairment in children with CKD than their non-CKD peers [34]. This finding underscores the major impact CKD has not only on mortality but also on the QOL of children [43]. In the study by Gerson et al [40], an assessment of HRQOL was conducted in children aged 2 to 16 years with mild to moderate CKD using PedsQL. Again, young subjects with CKD had significantly lower physical, school, emotional and social domain scores than their healthy counterparts. Short stature was also associated with lower scores in the physical functioning domain. These findings should serve as 'warning signals' for the clinician to initiate early interventions aimed to improve linear growth and normalize height in children with CKD [44]. The effect of ESRD on HRQOL in children is also significant. Although children with ESRD and their parents report lower HRQOL than do their healthy counterparts, the differences in HRQOL for paediatric patients treated with different modalities of RRT appear less conclusive [45].

A recent study by Diseth et al suggests that mental health, psychosocial adjustment, and QOL of children after renal transplantation are significantly impaired on both self-reports and proxy-reports compared with those of healthy controls [46]. The authors used the PedsQL and the Strength and Difficulties Questionnaire (SDQ-20) to assess the mental health of children aged 3 to 19 years while each mother's own mental health and QOL were assessed by the General Health Questionnaire (GHQ-30) and the Quality of Life Scale (QOLS). These findings were similarly reported by other workers who used PedsQL as instrument of HRQOL assessment [47, 48]. Mental health problems and psychosocial dysfunction can persist several years after diagnosis of CKD and treatment with RRT which affect the child's QOL and parental functioning [46].

Table 1. *Studies on Health-related Quality of Life (HRQOL) assessment in children with chronic kidney disease (CKD): Summary of findings*

STUDY	STAGE OF CKD	HRQOL INSTRUMENTS	MAJOR FINDINGS
-Gerson et al [40]	Mild to moderate CKD	PedsQL	- Lower overall HRQOL scores
-Diseth et al [46]	Post renal transplantation	PedsQL, SDQ-20, GHQ-30, QOLS	- Lower HRQOL at 2 to 16 years
-Varni et al [49]	End-stage Renal Disease (ESRD)	PedsQL	-Lower HRQOL (Patients on HD scored lower than post TX patients)
-McKenna et al [50]	End-stage Renal Disease (ESRD)	PedsQL	-Lower HRQOL scores in all domains (HD and PD patients scored the same)
-Goldstein et al [51]	End-stage Renal Disease (ESRD)	PedsQL	-Lower HRQOL scores in all domains (Post TX patients scored higher than HD/PD patients)
-Chiu et al [52]	End-stage Renal Disease (ESRD)	7- domain HRQOL questionnaire	- No difference between HRQOL scores of APD and post TX patients

HD= hemodialysis, PD= peritoneal dialysis, TX=renal transplantation, APD=automated PD

In the survey of 96 children with ESRD using the PedsQL 4.0 Generic Core Scales, Varni and co-workers documented that children with the disease self-reported impaired HRQOL as compared with healthy children [49]. In addition, patients on hemodialysis (HD) self-reported significantly lower over-all HRQOL and physical health as compared with those who underwent renal transplantation. McKenna et al used the PedsQL Generic Core Scales to measure HRQOL in 64 children with late stage CKD, and reported that the patients scored lower in all domains than did the healthy controls [50]. They also found no significant differences for children on HD as compared with those on peritoneal dialysis (PD). Children on dialysis reportedly scored equal to or higher than the renal transplantation group in all domains. Similarly, Goldstein et al in their study of children with ESRD using the PedsQL Generic Core Scales noted that the patients scored lower in all domains when compared to healthy controls [51]. Furthermore, patients who underwent renal transplantation (TX) reported better physical and psychosocial health than did dialysis patients. On the other hand, Chiu and colleagues did not document any significant difference between the HRQOL scores of automated PD (APD) patients and those who received renal transplantation [52]. They studied HRQOL in 42 paediatric patients with ESRD using their Chinese 7-domain HRQOL questionnaire adapted from the PedsQL. Although there appears to be no unanimity in the findings from these studies, patients who undergo renal transplantation and their parents generally score higher in HRQOL assessments than do dialysis patients which suggests a better QOL outcome for children receiving this treatment modality. However, the study by Diseth et al [46] demonstrated that mental health problems and psychosocial functioning can persist several years after treatment with renal transplantation (TX) affecting both the child's QOL and parental functioning.

Their observations bring to the fore the role of counseling in improving HRQOL as optimal treatment and follow-up of such patients require close collaboration between paediatricians and psychosocial experts. It has thus been recommended that professional mental health guidance which includes developmental and family perspectives should be offered routinely to renal transplantation patients and their parents [46]. The major findings of these studies are summarized in Table 1.

Despite the dependability of QOL measures in improving outcome variables in children with CKD, most clinicians rarely use them in clinical practice. The skepticism that greets their true value in patient management may be due to the plethora of available HRQOL instruments (each with different units of measurement) which gives room for interpretation challenges [42], as well as the belief by clinicians that clinical judgment is superior to formal assessment of QOL. Therefore, a continuous improvement on the available HRQOL instruments- to make them as simple as possible- may encourage clinicians to use them beyond the clinical trial setting. For now, this paradigm of using HRQOL assessment as an adjunct to RRT largely resides in the realm of research especially in most developing countries.

Conclusions

In children with mild/moderate CKD and ESRD, assessment of HRQOL is a useful and important clinical meas-

ure to monitor their well-being and functional status. Although an ESRD-specific HRQOL instrument for children is yet to be developed, the PedsQL is the commonly used generic HRQOL tool in QOL assessment. All the studies reviewed consistently show significantly lower HRQOL scores in children with mild/moderate CKD and ESRD when compared with their healthy counterparts. In future, a paediatric ESRD-specific instrument is needed to address differences in HRQOL between children on HD or PD and those who have received kidney transplantation. Despite the limitations of HRQOL assessment, its reliability as a clinical measure aimed to improve QOL outcomes in these patients is clearly evidence-based. Nevertheless, simplifying the available instruments may improve their acceptability among clinicians managing paediatric patients with CKD. There is an urgent need to make the assessment tools more user-friendly and patient-compliant. The clinician should also be able to interpret the scores more easily.

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Authors' contributions: SNU conceived the topic of the review, conducted the literature search and drafted the initial manuscript. VUM made substantial contributions to the revised draft. Both authors read and approved the final draft.

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Correspondence to:

SN Uwaezuoke
Department of Paediatrics
UNTH Ituku- Ozalla Enugu
Nigeria