Title:

Alterations in symptoms and health-related quality of life as kidney function deteriorates: A cross-sectional study

Running title:

Symptoms and quality of life in kidney disease

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ABSTRACT

Aims and objectives: To compare symptoms and health-related quality of life and to examine the relationship between these as kidney function deteriorates.

Background: Chronic kidney disease is a global health problem, and while knowledge of symptom burden and health-related quality of life is understood in kidney failure (previously end stage kidney disease), there is limited understanding about symptoms and health-related quality of life across the chronic kidney disease trajectory.

Design: Cross-sectional design reported using the STROBE guidelines.

Methods: 886 adults with varying levels of kidney function (chronic kidney disease grades 3b–5 including those receiving dialysis) completed the renal version of the Integrated Palliative care Outcome Scale and the Quality of Life Short Form-36 version 2. Socio-demographic and renal characteristics were also collected. Data were analysed using descriptive and inferential statistics.

Results: Participants had a mean age of 57 years and were mostly male. Regardless of chronic kidney disease grade, pain, poor mobility, weakness, anxiety and depression were the most prevalent and severe symptoms reported. Health-related quality of life was significantly associated with physical and psychological symptom scores. As kidney function deteriorated, both physical and mental health-related quality of life decreased, and prevalence and severity of symptoms increased.

Conclusions: There is substantial symptom burden irrespective of chronic kidney disease grade, which overwhelmingly affects health-related quality of life. Early identification by nurses would enable proactive management plans to be implemented.

Relevance to clinical practice: Nurses, whether in specialist renal services or in primary healthcare are ideally placed to regularly assess symptoms and health-related quality of life in those with chronic kidney disease. Timely assessment could assist in the targeting of earlier interventions designed to reduce symptom burden and to increase health-related quality of life.

KEYWORDS

Chronic kidney disease, dialysis, health-related quality of life, quality of life, symptoms

IMPACT STATEMENT

What does this paper contribute to the wider global clinical community?

- People experience poor health-related quality of life even at early chronic kidney disease grades due to substantial symptom burden and deterioration in physical functioning.
- Nurses ought to assess those with chronic kidney disease proactively and routinely for symptoms and health-related quality of life so that symptom management can be implemented swiftly.

INTRODUCTION

Chronic kidney disease (CKD) is one of the major global health problems, affecting 10–15% of the adult population (Mandayam & Winkelmayer, 2017) via irreversible damage to kidney function over at least a three-month period (Webster et al., 2017). Depending on the level of kidney function, CKD is classified into five grades, G1–G5 (G3 is sub-divided into G3a and G3b). The final grade (G5) was previously called end stage kidney disease but is now termed kidney failure (Levey et al., 2020). Once kidney failure is reached, collaborative decisions between individuals, family, and the multidisciplinary kidney team are made about whether to commence kidney replacement therapy (either haemodialysis [HD], peritoneal dialysis [PD] or kidney transplantation) or to receive conservative (supportive) care (Webster et al., 2017).

Symptoms are a multidimensional subjective experience and can be assessed on their occurrence (prevalence), frequency, severity, and distress (Almutary et al., 2013). People with the early CKD grades (i.e., CKD G1-3a) are often asymptomatic (Rosanky, 2012), however as kidney function deteriorates, uraemic wastes accumulate and people begin to experience both physical and psychological symptoms (Webster et al., 2017). As kidney function continues to deteriorate, symptoms become increasingly more burdensome which then impacts on everyday life (Almutary et al., 2016b). Health-related quality of life (HRQoL) is a multifaceted phenomenon that comprises the physical, psychological, social, and spiritual aspects of a person's life that are influenced by health, disease and treatments (Ferrans et al., 2005). As CKD affects many spheres of a person's life, early identification of symptoms could assist clinicians to implement strategies to improve the HRQoL of those afflicted.

BACKGROUND

People with kidney failure, including those receiving dialysis, experience a wide range of physical as well as psychological symptoms with the most prevalent symptoms being fatigue, drowsiness, pain, depression and anxiety (Almutary et al., 2013; Murtagh et al., 2007; Palmer et al., 2013). These symptoms are mediated via several factors such as the effects of CKD, its various treatments and the presence of comorbidities (Almutary et al., 2016a). For example, previous studies report that over 70% of those with CKD experience fatigue (Gregg et al., 2019; Jhamb et al., 2013) which could be due to anaemia, malnutrition, receiving HD, sleep disorders, and depression (Davey et al., 2019).

Findings from a systematic review of 19 studies suggest that CKD is associated with substantial symptom burden (Almutary et al., 2013), which is similar to or greater than the symptom burden experienced by people with terminal cancer (Bostwick et al., 2017; Solano et al., 2006). Fatigue, pain, irritability and sexual problems are particularly burdensome symptoms in CKD (Abeywickrama et al., 2020; Almutary et al., 2016a; Senanayake et al., 2017). Almutary et al. (2016a) compared the symptom burden of people receiving dialysis (G5D) with those with advanced kidney disease (G4 and G5) though not on dialysis and reported that those in the G5D group experienced greater symptom burden. However, few studies have compared symptom burden in early CKD grades (Lee & Jeon, 2015; Peng et al., 2017).

Impaired HRQoL is also common in people with CKD, particularly those receiving HD (Alam et al., 2019; Kalfoss et al., 2019; Premadasa et al., 2019). These impairments could be due to the increasing burden of symptoms, older age, advanced CKD grade, presence of comorbidities, prolonged duration of receiving dialysis as well as the functional limitations

associated with kidney failure (Almutary et al., 2017; Brkovic et al., 2016; Raj et al., 2017). Several studies that investigated HRQoL at different CKD grades have found that there was a declining trend in HRQoL across the disease trajectory (Aggarwal et al., 2016; Kefale et al., 2019; Krishnan et al., 2020; Peng et al., 2017). Understanding the pattern of HRQoL across the disease trajectory would help clinicians to better support people who are at risk of experiencing impairments in HRQoL so that care to improve their wellbeing can be commenced proactively.

Several studies have reported that greater symptom burden is the main contributor to poor HRQoL in people with CKD (Almutary et al., 2017; Jung & Kim, 2019). Although the participants in these two studies were limited to those with CKD G4, G5 and G5D, both studies found that a decrease in HRQoL when symptoms increased. As highlighted in a recent systematic review (Yapa et al., 2020), more studies are needed to investigate how symptoms and HRQoL change across the CKD trajectory. This study, therefore, aimed to compare symptom burden and HRQoL and to examine the relationship between these at CKD G3b, G4, G5 and G5D.

METHODS

Study design

Cross-sectional design reported using the Strengthening the Reporting of Observational studies in Epidemiology (STROBE; see Supplementary File 1; von Elm et al., 2007).

Participants and setting

This study was undertaken in renal outpatient clinics, renal wards and the HD unit at the Anuradhapura Teaching Hospital, Sri Lanka between October 2018 and January 2019. Adults

with a known diagnosis of CKD, who were able to understand Sinhalese (language) were recruited into this study using convenience sampling. Those with medically determined cognitive impairment and/or acute illness (such as peritonitis, myocardial infarction or respiratory infection) were excluded.

Sample size

The sample size for this study was based on a 5% type 1 error for 15% estimated prevalence of CKD in Anuradhapura district, Sri Lanka (Jayatilake et al., 2013). Accordingly, a sample size of 196 was required for each group (i.e., CKD G3b, G4, G5 and G5D). The final sample was increased by 15% to account for non-response data, which resulted in an overall sample size of 900.

Data collection

A self-report socio-demographic instrument was used to collect age (years), gender, level of education, occupation and monthly household income. Additionally, renal clinical information (past medical history and kidney replacement therapy information) was extracted from hospital records. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Levey et al., 2020) was used to calculate estimated glomerular filtration rate (eGFR) to determine CKD grade.

Assessment of symptoms and HRQoL

A self-report renal version of the Integrated Palliative care Outcome Scale (IPOS-renal) was used to assess common symptoms experienced during the past three days (Cicely Saunders Institute, 2012). The instrument assesses 15 physical and two psychological symptoms. Each item is scored using a five-point Likert scale. The physical symptom score ranges from 0 to

60, with zero being ‘no physical symptoms experienced’ and 60 being ‘worst experience of physical symptoms’. The psychological symptom score ranges from 0 to 8; a higher score reflects worse experience of psychological symptoms. The original version of the IPOS-renal has good reliability, with a Cronbach’s alpha value of 0.84 (Raj et al., 2018), and is widely used internationally (Morton et al., 2018; Purtell et al., 2018). However, as the IPOS-renal had not previously been used in Sri Lanka, it was translated into Sinhalese using a forward and backward translation technique prior to the study. The Cronbach’s alpha for the Sinhalese version of the IPOS-renal was 0.79.

The Short Form-36 health survey version 2 (SF-36v2) assesses HRQoL during the previous four weeks. This instrument contains eight sub-scales: (1) physical functioning, (2) role-physical, (3) bodily pain, (4) general health, (5) vitality, (6) social functioning, (7) role-emotional, and (8) mental health (Ware & Sherbourne, 1992). Furthermore, the SF-36v2 is divided into two summary scores, the total physical component summary (PCS) and the total mental component summary (MCS; Ware, 2000). Each item was scored using a Likert scale. The total score of the SF-36v2 ranges from 0 to 100; with a higher score indicating better HRQoL (Ware & Sherbourne, 1992). The SF-36v2 has been extensively used in various patient populations including CKD. It has also been translated into Sinhalese. The Sinhalese version of the SF-36v2 has good reliability, with a Cronbach’s alpha value of more than 0.8 for each sub-scale (Gunawardena et al., 2003).

Procedures

Potential participants were identified with the assistance of nursing staff in the renal department of the hospital. Before approaching potential participants, their eligibility and CKD grade were screened by accessing their hospital records. The eligibility of all

participants was screened by the lead author. Using a structured survey, the researcher or trained research assistants recruited participants and collected the data via an interviewer-administered method. Questions were read aloud to participants who had reading difficulties.

Ethical considerations

Ethical approval was received from the Ethics Review Committee, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka (Approval Number: ERC/2018/23) and the Human Research Committee, Queensland University of Technology (Approval Number: 1800000811). Informed consent was obtained from all participants prior to data collection.

Data analysis

Data were analysed using the Statistical Package for Social Sciences (IBM SPSS™) statistics version 23.0 (IBM Corp., 2015). Frequencies with percentages were calculated for categorical variables. For continuous variables, mean and standard deviation (SD) or median and interquartile range (IQR) were computed. All variables were normally distributed with the exception of eGFR and vomiting. Associations between categorical variables were examined by Pearson's χ^2 tests. Analysis of variance (ANOVA) tests were used to compare scores of the components and the overall scores of the instruments by CKD grade. In cases where normality assumptions were violated, Kruskal-Wallis tests were performed. Mean differences across CKD grades were investigated using ANOVA and post hoc tests (Tukey's a-b) if homogeneity of variance was not violated. The relationship between symptom scores and HRQoL was examined by linear regression model. The variables included to predict HRQoL scores in the model were age, gender, level of education, working status, monthly household income, number of comorbidities, CKD grade and physical/psychological symptom scores. Residuals of continuous explanatory variables included in the model were

normally distributed with constant variance. According to the standardised procedure for analysis of the SF-36v2, sub-scale scores and summary scores were computed using the Health Outcome Scoring Software 5.0 (Maruish, 2011). For symptoms, the total physical symptom score was computed by summating individual responses of 15 physical symptoms (Cicely Saunders Institute, 2012). The aggregated score of responses related to anxiety and depression represented the total psychological symptom score. Significance levels were set at p values ≤ .05. For multiple comparisons, p values were adjusted using Bonferroni correction method (Kirkwood & Sterne, 2003).

RESULTS

Participants' characteristics

A total of 886 participants took part in this study. The mean age of participants was 57.10±11.08 years (range: 18–84 years). The majority were men (68.4.%). Participants receiving dialysis (HD: n = 204; PD: n = 15) were slightly younger (49.68±10.92) than those in other CKD grades. More than half of participants had a level of education up to grade eight. Of the 393 participants who were still working, the majority had CKD G3b (n = 123). Only 11% of participants had a monthly household income over 25,000LKR (equivalent to AU $185). Approximately 80% of participants had at least one chronic disease. Participant characteristics are summarised in Table 1.

Symptoms across chronic kidney disease grades

Overall, the prevalence of symptoms increased with the progression of CKD grades (see Supplementary Table 1) and the most prevalent physical symptoms were pain, poor mobility, and weakness. In terms of psychological symptoms, over 80% of participants reported having symptoms of depression and anxiety. All of the symptoms, except weakness, shortness of

breath, and itching, were significantly associated with CKD grade ($p < .05$). Those with CKD G5D had significantly greater pain, dry mouth, difficulty sleeping, restless legs, changes in skin, diarrhoea, vomiting, depression, and anxiety ($p < .001$).

The total physical and psychological symptom scores significantly increased from CKD G3b to G5D ($p < .001$). Pain, poor mobility and weakness were the three most severe physical symptoms reported across CKD grades. Overall, there were significant differences in mean severity of symptoms except for drowsiness, shortness of breath, itching and constipation across CKD grades ($p < .05$). On average, greater severity of physical symptoms was experienced by those with CKD G5. With respects to psychological symptoms, severity of depression and anxiety was greatest in those receiving dialysis. Post hoc analysis found that mean severity of poor mobility, weakness, dry mouth, poor appetite, difficulty sleeping, nausea, changes in skin, and vomiting in those with CKD G5 was significantly higher than that experienced by those in the CKD G3b group ($p < .05$). Symptom severity across CKD grades is shown in Table 2.

Health-related quality of life across chronic kidney disease grades

Mean total, PCS and MCS scores decreased from CKD G3b to G5. Overall, there were significant differences in mean total PCS and all sub-scale scores except for general health across CKD grades ($p < .001$). Compared to those with CKD G3b, participants with CKD G5 had significantly lower scores for total PCS, physical functioning, role-physical, bodily pain, and vitality ($p < .05$) although those receiving dialysis had significantly higher mean scores for total PCS, role-physical, bodily pain, and role-emotional sub-scales than those with CKD G5 ($p < .001$). There were no significant differences in mean total MCS scores across CKD grades. Table 3 presents the HRQoL scores across CKD grades.

Predictors of health-related quality of life

Age, working status, CKD grade, number of comorbidities, and the total physical symptom score were significant predictors of total PCS score ($F_8 = 66.89$, $p < .001$), explaining 37% deterioration of physical HRQoL (see Supplementary Table 2). Gender, level of education, monthly income, and the total psychological symptom score did not significantly influence total PCS score. The total physical symptom score was the strongest predictor of total PCS score (B = -0.58; 95% CI: -0.65, -0.51; $p < .001$) followed by age (B = -0.11; 95% CI: -0.16, -0.07; $p < .001$). Compared to those with CKD G3b, participants with CKD G4 (B = -2.79; 95% CI: -4.17, -1.41; $p < .001$), G5 (B = -2.27; 95% CI: -3.68, -0.86; $p < .05$) and G5D (B = -1.48; 95% CI: -2.83, -0.14; $p < .05$) had significantly lower total PCS scores. Having a job was associated with significantly higher total PCS score (B = 3.31; 95% CI: 2.38, 4.23; $p < .001$). Those with only one chronic disease had a significantly higher total PCS score compared with those with ≥ 2 comorbidities (B = 1.36; 95% CI: 0.35, 2.37; $p < .05$).

Monthly household income, CKD grade and the total physical and psychological symptom scores significantly predicted total MCS score ($F_8 = 66.89$, $p < .001$); these explained 28% of the variation seen in the deterioration of mental HRQoL (see Supplementary Table 3). Age, gender, level of education, working status, and number of comorbidities were not significantly associated with total MCS score. Those with a monthly income < 5000 LKR had significantly lower total MCS scores compared to those earning > 25,000 LKR (B = -2.83; 95% CI: -4.76, -0.90; $p < .05$) per month. Compared to those with CKD G3b, participants with CKD G5 (B = -1.52; 95% CI: -2.90, -0.14; $p < .05$) and G5D (B = -2.01; 95% CI: -3.40, -0.62; $p < .05$) had significantly lower total MCS scores. Both physical (B = -0.34; 95% CI: -

0.42, -0.27; $p < .001$) and psychological (B = -1.62; 95% CI: -1.90, -1.34; $p < .001$) symptom scores were associated with significantly lower total MCS score.

DISCUSSION

This study compared the symptom burden and HRQoL of people with CKD and examined the relationship between these at different CKD grades. Overall, as the disease progressed from CKD G3b to G5D, both physical and mental HRQoL gradually decreased along with a slow rise in symptom severity. This finding emphasises a negative relationship between symptoms and HRQoL across the CKD trajectory. The participants of this study were, however, relatively younger (by a decade) and had fewer comorbidities when compared to people with CKD from other countries (see for example Nguyen et al., 2018; Zimbudzi et al., 2020). Nevertheless, substantial symptom burden and impaired HRQoL was experienced even at this younger age. Considerable physical limitations due to increased symptom burden can have a negative impact in those of working age and could lead to financial stress. Routine clinical assessment for symptoms would assist in identifying severe symptoms sooner to maintain overall wellbeing.

Pain, poor mobility, weakness, depression, and anxiety were the most reported and severe symptoms in this study. In contrast, other studies report different symptoms (fatigue, muscle strain, and sexual problems) to be the most severe (Almutary et al., 2016a; Karasneh et al., 2020; Senanayake et al., 2017). The differences in symptoms may be due to heterogeneity between studies, the use of different instruments, and the context. Furthermore, in this study, participants were more likely to report burdensome symptoms depending on whether they worked in physically demanding jobs (e.g., farming). Nevertheless, given the importance of delivering person-centred care, assessment of not only symptom occurrence but also

symptom severity is needed because severity reflects the magnitude of the impact of symptoms on the everyday life of those with CKD.

Across CKD G3b to G5, both physical and mental HRQoL scores were lower than that of healthy population norms and both of these also decreased as kidney function declined. In contrast to other studies (Alam et al., 2019; Kalfoss et al., 2019; Krishnan et al., 2020), participants in this study who were receiving dialysis (either HD or PD) experienced slightly better physical HRQoL than those with CKD G5. This relatively higher total PCS score could be due to the younger age and higher percentage of men in the G5D group. Considering the lifelong nature of CKD and the complexity of dialysis therapy, another possible explanation for better total PCS scores for those receiving dialysis is that they may have adapted to life with dialysis therapy. This phenomenon is known as response shift (Sprangers & Schwartz, 1999), and could reflect that those receiving dialysis may have internally reviewed their life goals to align with the demands of dialysis treatment as well as their changing (deteriorating) health. In our study, given the context in an agricultural region, everyday activities would have to change to those which require less physical energy as they would be less able to perform physically demanding farming work, and further research will be needed to explore role change and financial stress of CKD.

Overall, we found that the physical component of HRQoL deteriorated more than that of the mental component as kidney function worsened. This lower total PCS score could be due to greater physical symptom burden and increased functional limitations associated with CKD progression (Almutary et al., 2017). The slight deterioration of the total MCS score may be explained by people's changing expectations to align with lower HRQoL states when adjusting to life with CKD over time (Ferrans, 2007). For nurses working in primary

healthcare or outpatient areas, even those with CKD G3b ought to be assessed for HRQoL, so that strategies to support people's physical and mental wellbeing can be incorporated into individualised care plans.

The physical component of HRQoL, in this study, was predicted by CKD grade, the total physical symptom score, age, working status, and the number of comorbidities. These findings are consistent with other studies (Almutary et al., 2017; Jung & Kim, 2019; Senanayake et al., 2020). As kidney function deteriorates, those with advanced CKD grades are more likely to experience impairments in physical HRQoL due to increased symptom burden and physical ramifications (Almutary et al., 2017; Jung & Kim, 2019; Ng et al., 2020). We also found that comorbidity load was associated with poorer HRQoL, and participants with fewer chronic diseases experienced better physical HRQoL. While each chronic disease has specific symptoms, many symptoms are common with CKD. Collectively, these symptoms may contribute to the overall experience of symptom load in those with CKD. As such, having fewer chronic diseases inflicts less strain on symptom load and physical functioning (Tonelli et al., 2015), which may explain the better total PCS score reported by those with few comorbidities. Participants who were still working were also more likely to experience better HRQoL than those not employed. While experiencing a debilitating disease such as CKD, retaining the ability to work, earn an income and contribute to the household budget may account for the better HRQoL of those employed.

Physical and psychological symptoms, CKD grade, and monthly household income predicted the mental health aspects of HRQoL. While psychological symptoms and low income are known to impair HRQoL (Abeywickrama et al., 2020; Kefale et al., 2019), this study also found that physical symptoms (pain and poor mobility) correlated with a reduction in the total

MCS scores. These physical symptoms, in particular, could limit participation in everyday social activities and contribute to decreased emotional wellbeing leading to lower overall mental HRQoL. Financial constraints experienced due to losing work such as being unable to undertake heavy or strenuous work (e.g., farming) are likely to lead to additional difficulties in managing everyday expenses which would also impact on mental health and wellbeing. Strategies to support the mental wellbeing of people with CKD ought to be considered an important component of nursing practice.

Limitations of the study

The study has some limitations. The sample was drawn from one site, although the selected hospital is the largest tertiary level hospital in the agricultural region of Sri Lanka, where the prevalence of CKD is high. Despite the large sample size across CKD G3b–G5D, the use of a cross-sectional design limits the prediction of causality between symptoms and HRQoL in CKD and may limit the generalisability of study results. As self-report measures were used, participants could have under or overrated their responses to items in the study measures, however, given the subjective nature of symptoms and HRQoL, these patient-reported outcome measures used in this study were appropriate.

CONCLUSION

Overall, results indicated that people experience poor HRQoL while experiencing considerable symptom burden at early stages of the disease and prior to the terminal phase of CKD (i.e., G5). Both physical and mental HRQoL decreased as symptoms increased in line with the progression of the disease. Therefore, regardless of CKD grade, symptom (presence of and severity) and HRQoL assessments ought to occur routinely, and nurses working in

either primary or hospital care settings could perform these assessments. Targeted interventions are also needed much earlier in the CKD trajectory.

RELEVANCE TO CLINICAL PRACTICE

Given the insidious nature of the disease trajectory, those with CKD G3b ought to be assessed for symptom burden and HRQoL at six- or twelve-month intervals using validated assessment instruments. However, as those who have advanced CKD grades (i.e., G4, G5 and G5D) experience higher symptom burden and lower HRQoL compared to those with CKD G3b, more frequent assessments may be warranted (approximately three to six monthly). These regular assessments could help nurses and other members of the multidisciplinary healthcare team to identify people who need increased attention so that prompt, timely and person-centred interventions can be implemented to relieve symptom burden. Moreover, the identification of these people will help clinicians to make referrals to relevant support services (e.g., social services), which may assist managing the physical and mental health changes occurring with CKD. Those who are older, unemployed, experiencing greater symptom burden, have an advanced CKD grade, or who have more comorbidities need increased attention to assist the implementation of timely interventions that target those with unmet needs to improve their wellbeing.

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Table 1. Socio-demographic and clinical characteristics by CKD grade (N = 886)

Characteristics	Overall N (%)	G3b (n = 224) N (%)	G4 (n = 222) N (%)	G5 (n = 221) N (%)	G5D (n = 219) N (%)	Overall Significance
Age (Years)						$p < .001^{*}$
Mean (SD)	57.10 (11.08)	55.96 (10.97)	61.86 (8.86)	60.82 (9.02)	49.68 (10.92)	
Gender						$p < .001^{**}$
Male	606 (68.40)	136 (60.71)	133 (59.91)	157 (71.04)	180 (82.19)	
Female	280 (31.60)	88 (39.29)	89 (40.09)	64 (28.96)	39 (17.81)	
Level of education						$p < .001^{**}$
Up to grade 8	521 (58.80)	118 (52.68)	152 (68.47)	145 (65.61)	106 (48.40)	
Up to Ordinary Level (grade 9–11)	257 (29.01)	79 (35.27)	50 (22.52)	52 (23.53)	76 (34.70)	
Up to Advanced Level (grade 12–13)	94 (10.61)	25 (11.16)	18 (8.11)	19 (8.60)	32 (14.61)	
Diploma or above	14 (1.58)	2 (0.89)	2 (0.90)	5 (2.26)	5 (2.28)	
Working						$p < .001^{**}$
Yes	393 (44.36)	123 (54.91)	103 (46.40)	101 (45.70)	66 (30.14)	
No	493 (55.64)	101 (45.09)	119 (53.60)	120 (54.30)	153 (69.86)	
Monthly income (LKR)						$p < .001^{**}$
Less than 5,000	131 (14.79)	26 (11.61)	42 (18.92)	46 (20.82)	17 (7.76)	
5,001–10,000	315 (35.55)	72 (32.14)	85 (38.29)	73 (33.03)	85 (38.81)	
10,001–25,000	341 (38.49)	87 (38.84)	80 (36.04)	85 (38.47)	89 (40.64)	
More than 25,000	83 (11.17)	39 (17.41)	15 (6.75)	17 (7.68)	28 (12.79)	
eGFR† (ml/min/1.73m^2)						$p < .001^{***}$
Median (IQR)	21.94 (21.66)	38.54 (8.70)	21.66 (7.60)	8.87 (5.81)	-	
Number of comorbidities						$p < .001^{**}$
0	181 (20.43)	61 (27.23)	56 (25.23)	52 (23.53)	12 (5.48)	
1	378 (42.66)	79 (35.27)	78 (35.14)	93 (42.08)	128 (58.45)	
2 or more	327 (36.91)	84 (37.50)	88 (39.63)	76 (34.39)	79 (36.07)	

Note: †eGFR cannot be calculated for G5D due to elimination of creatinine and urea during dialysis; $^{*}p$ value based on ANOVA test; $^{**}p$ value based on Pearson's χ^2 test; $^{***}p$ value based on Kruskal-Wallis test; eGFR = estimated glomerular filtration rate; IQR = Interquartile range; LKR = Sri Lankan rupees; SD = standard deviation

Table 2. IPOS-renal symptom severity by CKD grade (N = 886)

Symptom	Overall Mean (SD)	G3b Mean (SD)	G4 Mean (SD)	G5 Mean (SD)	G5D Mean (SD)	Overall Significance
Physical						
Pain	1.80 (1.00)	1.82 (1.00)	1.97 (0.96)	1.89 (0.99)	1.50 (1.03)	$p < .001^{*}$
Poor mobility	1.45 (1.10)	1.14 (1.04)	1.57 (1.04)	1.62 (1.10)	1.48 (1.17)	$p < .001^{*}$
Weakness	1.38 (1.07)	1.13 (1.01)	1.37 (1.00)	1.55 (1.03)	1.48 (1.18)	$p < .001^{*}$
Dry mouth	1.14 (1.06)	0.87 (0.91)	0.90 (0.97)	1.21 (1.07)	1.57 (1.16)	$p < .001^{*}$
Drowsiness	1.06 (1.01)	1.00 (0.97)	1.04 (0.97)	1.21 (1.04)	1.00 (1.03)	NS
Poor appetite	1.17 (1.20)	0.83 (1.08)	1.00 (1.12)	1.43 (1.17)	1.44 (1.30)	$p < .001^{*}$
Difficulty sleeping	1.09 (1.13)	0.83 (1.05)	0.98 (1.04)	1.15 (1.20)	1.40 (1.17)	$p < .001^{*}$
Restless legs	0.60 (0.86)	0.67 (0.91)	0.70 (0.92)	0.76 (0.91)	0.25 (0.58)	$p < .001^{*}$
Shortness of breath	0.58 (0.86)	0.50 (0.79)	0.54 (0.83)	0.58 (0.79)	0.73 (0.99)	NS
Itching	0.54 (0.82)	0.50 (0.75)	0.46 (0.83)	0.67 (0.93)	0.52 (0.73)	NS
Nausea	0.53 (0.84)	0.37 (0.70)	0.49 (0.79)	0.70 (0.89)	0.58 (0.93)	$p < .001^{*}$
Constipation	0.70 (0.94)	0.59 (0.94)	0.69 (0.95)	0.79 (0.97)	0.70 (0.91)	NS
Changes in skin	0.34 (0.70)	0.21 (0.56)	0.26 (0.62)	0.40 (0.79)	0.52 (0.77)	$p < .001^{*}$
Diarrhoea	0.32 (0.69)	0.13 (0.45)	0.21 (0.58)	0.27 (0.65)	0.68 (0.87)	$p < .001^{*}$
Vomiting	0.26 (0.61)	0.23 (0.60)	0.29 (0.64)	0.37 (0.69)	0.16 (0.50)	$p < .001^{**}$
Psychological						
Depression	1.61 (0.95)	1.34 (0.93)	1.45 (0.92)	1.55 (1.00)	2.12 (0.73)	$p < .001^{*}$
Anxiety	1.48 (1.00)	1.21 (0.96)	1.33 (0.99)	1.50 (1.02)	1.89 (0.88)	$p < .001^{*}$
Total physical symptoms score	12.97 (6.99)	10.83 (6.28)	12.49 (6.62)	14.60 (7.58)	14.00 (6.87)	$p < .001^{*}$
Total psychological symptoms score	3.09 (1.83)	2.55 (1.77)	2.78 (1.76)	3.05 (1.90)	4.01 (1.53)	$p < .001^{*}$

Note: $^{*}p$ value based on ANOVA; $^{**}p$ value based on Kruskal-Wallis test; SD = standard deviation; NS = non-significant

Table 3. Health-related quality of life (SF-36v2) scores by CKD grade (N = 886)

Domain	Overall Mean (SD)	G3b Mean (SD)	G4 Mean (SD)	G5 Mean (SD)	G5D Mean (SD)	Overall Significance
Total PCS	42.26 (8.42)	44.09 (7.46)	41.37 (8.04)	39.80 (8.67)	43.77 (8.79)	$p < .001^*$
Total MCS	44.52 (8.37)	45.36 (8.35)	44.63 (8.53)	44.09 (8.44)	43.98 (8.13)	NS
Physical functioning	44.95 (9.64)	48.31 (7.80)	44.24 (9.33)	42.87 (10.30)	44.34 (10.13)	$p < .001^*$
Role-physical	40.37 (11.29)	41.06 (9.92)	38.93 (11.16)	36.40 (10.54)	45.14 (11.72)	$p < .001^*$
Bodily pain	41.88 (8.48)	42.35 (8.48)	40.95 (8.00)	40.05 (7.99)	44.18 (8.91)	$p < .001^*$
General health	41.78 (8.12)	42.89 (8.03)	41.69 (6.98)	41.35 (8.09)	41.18 (9.19)	NS
Vitality	45.37 (7.56)	47.30 (7.34)	45.07 (7.40)	44.31 (7.88)	44.77 (7.32)	$p < .001^*$
Social functioning	42.13 (11.84)	44.58 (11.07)	43.38 (11.41)	41.66 (11.19)	38.82 (12.88)	$p < .001^*$
Role-emotional	43.42 (12.67)	42.79 (12.43)	41.54 (13.26)	40.32 (12.34)	49.13 (10.73)	$p < .001^*$
Mental health	44.46 (8.71)	46.37 (7.86)	44.94 (8.48)	44.75 (9.01)	41.74 (8.87)	$p < .001^*$

Note: $^*p$ value based on ANOVA; PCS = physical component summary; MCS = mental component summary; SD = standard deviation; NS = non-significant

Supplementary Table 1. IPOS-renal symptom prevalence by CKD grade (N = 886)

Symptom	Overall N (%)	G3b N (%)	G4 N (%)	G5 N (%)	G5D N (%)	Overall Significance
Physical						
Pain	748 (84.42)	191 (85.27)	200 (90.09)	190 (85.97)	167 (76.26)	$p < .001^*$
Poor mobility	649 (73.25)	139 (62.05)	177 (79.73)	174 (78.73)	159 (72.60)	$p < .001^*$
Weakness	629 (70.99)	143 (63.84)	162 (72.97)	172 (77.83)	152 (69.41)	$p < .05^*$
Dry mouth	538 (60.72)	123 (54.91)	119 (53.60)	140 (63.35)	156 (71.23)	$p < .001^*$
Drowsiness	535 (60.38)	135 (60.27)	134 (60.36)	146 (66.06)	120 (54.79)	NS
Poor appetite	487 (54.97)	94 (41.96)	114 (51.35)	146 (66.06)	133 (60.73)	$p < .001^*$
Difficulty sleeping	481 (54.29)	100 (44.64)	118 (53.15)	118 (53.39)	145 (66.21)	$p < .001^*$
Constipation	355 (40.07)	71 (31.70)	88 (39.64)	102 (46.15)	94 (42.92)	$p < .05^*$
Restless legs	333 (37.59)	92 (41.07)	97 (43.69)	104 (47.06)	40 (18.27)	$p < .001^*$
Shortness of breath	329 (37.13)	72 (32.14)	76 (34.23)	90 (40.72)	91 (41.55)	NS
Itching	313 (35.33)	79 (35.27)	65 (29.28)	86 (38.91)	83 (37.90)	NS
Nausea	297 (33.52)	54 (24.12)	72 (32.43)	98 (44.34)	73 (33.33)	$p < .001^*$
Changes in skin	195 (22.01)	30 (13.39)	37 (16.67)	52 (23.54)	76 (34.70)	$p < .001^*$
Diarrhoea	181 (20.43)	19 (8.48)	29 (13.06)	37 (16.74)	96 (43.84)	$p < .001^*$
Vomiting	162 (18.28)	33 (14.73)	45 (20.27)	59 (26.70)	25 (11.42)	$p < .001^*$
Psychological						
Depression	763 (86.12)	178 (79.46)	187 (84.23)	179 (81.00)	219 (100.00)	$p < .001^*$
Anxiety	726 (81.94)	166 (74.11)	173 (77.93)	179 (81.00)	208 (94.98)	$p < .001^*$

Note: $^*p$ value based on Pearson's χ^2 test; NS = non-significant

Supplementary Table 2. Predictors of total PCS (N = 886)

Variables	Fitted model	
	Regression coefficient (B)	95% Confidence interval
Constant	55.67**	52.97, 58.38
Age	-0.11**	-0.16, -0.07
Gender		
Male	0.67	-0.37, 1.71
Female	Ref	
Level of education		
Up to grade 8	-0.31	-4.04, 3.42
Up to Ordinary Level (grade 9–11)	-0.17	-3.91, 3.56
Up to Advanced Level (grade 12–13)	-0.44	-4.27, 3.38
Diploma or above	Ref	
Working		
Yes	3.31**	2.38, 4.23
No	Ref	
Monthly income (LKR)		
Less than 5,000	0.13	-1.87, 2.13
5,001–10,000	1.18	-0.53, 2.89
10,001–25,000	0.17	-1.46, 1.79
More than 25,000	Ref	
CKD grade		
G4	-2.79**	-4.17, -1.41
G5	-2.27*	-3.68, -0.86
G5D	-1.48*	-2.83, -0.14
G3b	Ref	
Number of comorbidities		
0	0.81	-0.44, 2.06
1	1.36*	0.35, 2.37
2 or more	Ref	
Total physical symptom score	-0.58**	-0.65, -0.51
Total psychological symptom score	-0.04	-0.31, 0.23
R^2	0.38	
Adjusted R^2	0.37	
F	66.89**	

Note: $^{*}p < .05$; $^{**}p < .001$; Ref = reference group; CKD = chronic kidney disease; LKR = Sri Lankan rupees

Supplementary Table 3. Predictors of total MCS (N = 886)

Variables	Fitted model	
	Regression coefficient (B)	95% Confidence interval
Constant	55.63**	53.62, 57.63
Age	0.05	-0.01, 0.10
Gender		
Male	-0.43	-1.49, 0.64
Female	Ref	
Level of education		
Up to grade 8	-1.18	-5.15, 2.79
Up to Ordinary Level (grade 9–11)	-1.69	-5.67, 2.28
Up to Advanced Level (grade 12–13)	-0.66	-4.73, 3.41
Diploma or above	Ref	
Working		
Yes	0.47	-0.63, 1.57
No	Ref	
Monthly income (LKR)		
Less than 5,000	-2.83*	-4.76, -0.90
5,001–10,000	-1.06	-2.71, 0.59
10,001–25,000	0.67	-0.93, 2.28
More than 25,000	Ref	
CKD grade		
G4	-0.92	-2.29, 0.45
G5	-1.52*	-2.90, -0.14
G5D	-2.01*	-3.40, -0.62
G3b	Ref	
Number of comorbidities		
0	-0.35	-1.72, 1.02
1	0.66	-0.43, 1.76
2 or more	Ref	
Total physical symptom score	-0.34**	-0.42, -0.27
Total psychological symptom score	-1.62**	-1.90, -1.34
R^2	0.28	
Adjusted R^2	0.28	
F	43.42**	

Note: $^{*}p < .05$; $^{**}p < .001$; Ref = reference group; CKD = chronic kidney disease; LKR = Sri Lankan rupees