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QUALITY OF LIFE IN PRE-DIALYSIS CHRONIC KIDNEY DISEASE: INFLUENCE OF GENDER, STAGE, SYMPTOM BURDEN, AND COMORBIDITIES

Costina GROZA, Emil CEBAN, Oleg ARNAUT, Boris SASU, Liliana GROPPA

Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Corresponding author: Costina GROZA, e-mail: grozacostina@gmail.com

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ABSTRACT

Introduction Chronic kidney disease (CKD) negatively affects health-related quality of life (HRQoL) even in the pre-dialysis stages. However, data regarding gender- and stage-related differences in Eastern European CKD populations remain sparse compared to major international cohorts like CRIC and DOPPS. In this study, Low quality of life (low QoL) was defined as a Physical Component Summary (PCS) score below the 25th percentile of the cohort distribution.

Materials and methods This cross-sectional study included 989 adults with CKD stages I–V undergoing conservative management. HRQoL was evaluated using the KDQOL-36™ questionnaire. We performed gender and CKD stage comparisons, Pearson correlations, and multivariate logistic regression to identify predictors of low QoL. Symptom burden was assessed via structured patient interviews, complemented by the KDQOL-36™ symptom domain to ensure standardized reporting.

Results The mean patient age was 58.3 ± 12.5 years, and 52.8% were male. The mean PCS and Mental Component Summary (MCS) scores were 40.2 ± 10.8 and 43.5 ± 11.2, respectively. Women had lower PCS scores than men (38.0 vs. 41.0; $p < 0.05$) and a higher prevalence of fatigue (95.0% vs. 85.0%) and dysuria (70.8% vs. 52.6%; $p < 0.001$). QoL declined progressively with advancing CKD stage (PCS 44.2 in stages I–II vs. 34.5 in stages IV–V; $p < 0.001$), and PCS correlated positively with eGFR ($r \approx 0.45$; $p < 0.001$). Independent predictors of low QoL included advanced CKD stage (OR 2.72), diabetes (OR 1.94), anemia (OR 1.80), hypoalbuminemia (OR 1.70), a disease duration of >5 years (OR 1.50), and female sex (OR 1.38).

Conclusions HRQoL is substantially impaired in pre-dialysis CKD, particularly among women and patients with advanced disease, highlighting the need for targeted, patient-centered interventions.

Keywords Chronic kidney disease, quality of life, KDQOL-36, gender, CKD stages, symptom burden, comorbidities.

CALITATEA VIEȚII ÎN BOALA CRONICĂ DE RINICHI ÎN STADIILE PRE-DIALITICE: INFLUENȚA GENULUI, A STADIULUI, A POVERII SIMPTOMELOR ȘI A COMORBIDITĂȚILOR

Introducere Boala cronică de rinichi (BCR) afectează negativ calitatea vieții, (HRQoL) chiar și în stadiile pre-dializă. Datele privind diferențele legate de gen și de stadiu, în populațiile cu BCR din Europa de Est, sunt limitate. Acest studiu abordează o lacună importantă în cunoaștere, deoarece datele privind determinanții HRQoL în populațiile cu BCR pre-dializă, din Europa de Est rămân limitate, în comparație cu cohortele internaționale majore, precum CRIC și DOPPS. Calitatea scăzută a vieții (QoL scăzută) în acest studiu a fost definită ca un scor al Sumarului Componentei Fizice (PCS) sub 25% de distribuție a cohortei.

Materiale și metode Un studiu transversal a inclus 989 de adulți cu boală cronică de rinichi (BCR) în stadiile I–V, aflați sub tratament conservator. Calitatea vieții legată de sănătate (HRQoL) a fost evaluată utilizând chestionarul KDQOL-36™. Au fost realizate comparații în funcție de gen și de stadiul BCR, corelații Pearson și regresie logistică multivariată pentru a identifica predictorii unei calități scăzute a vieții. Simptomele au fost evaluate prin interviuri structurate cu pacienții, completate cu itemi din domeniul simptomelor al chestionarului KDQOL-36™, pentru a asigura o raportare standardizată.

Rezultate Vârsta medie a fost de 58,3±12,5 ani, iar 52,8% dintre participanți au fost bărbați. Scorurile medii PCS și MCS au fost 40,2±10,8, respectiv 43,5±11,2. Femeile au avut scoruri PCS mai mici decât bărbații (38,0 vs. 41,0; $p<0,05$) și o prevalență mai mare a oboselii (95,0% vs. 85,0%) și a disuriei (70,8% vs. 52,6%; $p<0,001$). Calitatea vieții a scăzut odată cu progresia stadiului BCR, scorul PCS fiind 44,2 în stadiile I–II comparativ cu 34,5 în stadiile IV–V ($p<0,001$). Scorul PCS s-a corelat cu rata de filtrare glomerulară estimată (eGFR) ($r\approx0,45$; $p<0,001$). Predictorii independenți ai unei calități scăzute a vieții au fost: stadiul avansat al BCR (OR 2,72), anemia (OR 1,80), diabetul (OR 1,94), hipoalbuminemia (OR 1,70), durata bolii >5 ani (OR 1,50), sexul feminin (OR 1,38).

Concluzii HRQoL este substanțial afectată în BCR pre-dializă, în special în rândul femeilor și al pacienților cu boală avansată, evidențiind necesitatea unor intervenții direcționate, centrate pe pacient.

Cuvinte-cheie Boală cronică de rinichi, calitatea vieții, KDQOL-36, gen, stadii BCR, povara simptomelor, comorbidități.

INTRODUCTION

Chronic kidney disease (CKD) is a major global public health concern. It is estimated to affect approximately 10–13% of the adult population worldwide, corresponding to more than 800 million individuals (1). Its prevalence continues to increase, largely because of population aging and the growing burden of major risk factors such as diabetes and hypertension. CKD is also an increasingly important cause of mortality and disability: in 2017, it ranked as the 12th leading cause of death worldwide, and projections suggest that by 2040 it may become the 5th leading cause of years of life lost (2). Beyond its effect on survival, CKD has a substantial impact on patients' daily functioning and overall well-being. Across all stages, it is associated with increased cardiovascular morbidity, fatigue, and reduced quality of life (3). Health-related quality of life (HRQoL) has therefore become an important outcome in CKD care, as it reflects the physical, psychological, and social consequences of the disease (4). In patients with advanced CKD and in those receiving dialysis, HRQoL is often severely impaired– comparable to or worse than many other chronic illnesses. However, relatively fewer studies have focused on HRQoL in earlier, pre-dialysis stages of CKD (5). The period preceding dialysis is particularly important, as patients with advanced CKD often experience increasing symptom burden, uncertainty about disease progression, and growing lifestyle restrictions, all of which may adversely affect QoL. Identifying the determinants of QoL in pre-dialysis CKD is therefore essential for timely intervention (6).

Gender-related differences in CKD progression and outcomes are well documented. Although CKD is more prevalent in women, men are more likely to progress to end-stage kidney disease (7). Yet, women with CKD often report worse subjective health status and a greater symptom burden than men. Prior studies have shown that female patients more frequently experience fatigue, pain, and depressive symptoms, which may contribute to lower quality-of-life scores (8). On the other hand, male patients may under-report symptoms or face different psychosocial stressors. Further clarification is needed regarding the effect of sex on quality of life in CKD, particularly in the pre-dialysis setting, to support a more tailored, patient-centred care. Comorbidities and CKD-related complications are also important determinants of quality of life (6). Diabetes mellitus and cardiovascular disease are common in this population and contribute not only to faster disease progression, but also to poorer functional status and reduced QoL (9). CKD-related anemia, which is common in stages IV and V, is associated with fatigue, weakness, and cognitive impairment, all of which can markedly affect vitality and day-to-day functioning. Likewise, chronic inflammation and poor nutritional status, reflected in part by hypoalbuminaemia, are associated with worse physical and mental well-being (10). Previous studies have shown that greater symptom burden is associated with QoL in CKD, and that correction of potentially treatable factors, such as anaemia, may improve patient-reported outcomes (11). However, the relationship between CKD stage, symptom burden, and quality of life remains incompletely understood, particularly whether quality-of-life impairment in pre-dialysis CKD is driven mainly by disease severity, symptom burden, comorbid conditions, or broader psychosocial factors.

This study evaluated quality of life in a large cohort of pre-dialysis CKD patients across all disease stages (I–V) before the initiation of hemodialysis. The primary objective was to determine whether clinical severity and sex independently predict low HRQoL in pre-dialysis CKD. Secondary objectives were to assess differences in QoL between female and male CKD patients and to examine the relationship of QoL with clinical factors, including symptoms and common comorbidities. The study further aimed to identify the principal predictors of poor QoL in this population. It was hypothesized that

HRQoL in pre-dialysis CKD is significantly influenced by CKD stage, female sex, symptom burden, and major comorbidities (anemia, diabetes, and hypoalbuminemia), with advanced disease stages and female sex independently associated with low PCS scores.

MATERIAL AND METHODS

Patients were recruited consecutively during routine nephrology visits to minimize selection bias and to ensure adequate representation of the outpatient CKD population.

Study Design and Setting

This cross-sectional observational study included adult patients with CKD stages I–V who were receiving nephrology care at a tertiary referral center. Recruitment took place between 2022 and 2023 in the Nephrology Department of the Republican Clinical Hospital "Timofei Moșneaga" in Chișinău, Moldova. At the time of evaluation, all patients were managed conservatively and were not receiving dialysis. The study protocol, entitled *Quality of Life in Chronic Kidney Disease up to Hemodialysis*, was approved by the Research Ethics Committee of Nicolae Testemițanu University (approval No. 35, 2023). Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki and national guidelines for research involving human subjects.

Inclusion and Exclusion Criteria

Adult patients (aged ≥18 years) with CKD of any etiology in stages I through V (pre-dialysis) were included. CKD was defined and staged according to KDIGO criteria as persistent GFR <60 mL/min/1.73 m^2 or markers of kidney damage present for ≥3 months, with stages I–V determined by estimated GFR. Exclusion criteria were maintenance dialysis, a functioning kidney transplant, and any other end-stage non-renal illness expected to have a dominant effect on QoL (e.g. metastatic cancer, class IV heart failure, or advanced neurodegenerative disease). Patients with acute kidney injury and those unable to complete the QoL questionnaire because of cognitive or language barriers were also excluded. On the basis of prevalence data and the anticipated subgroup analyses, the target sample size was at least 450 patients to provide adequate statistical power. In total, 989 eligible patients were enrolled, reflecting a broad spectrum of CKD severity.

Data Collection

Clinical data were obtained from medical records and structured interviews. The following data were recorded: demographic characteristics (age, sex, education, employment, and residence), CKD etiology and duration, comorbidities (e.g., hypertension, diabetes, and cardiovascular disease), and recent laboratory parameters, including creatinine, urea, eGFR calculated using the 2021 CKD-EPI equation, hemoglobin, albumin, and proteinuria. CKD stages were classified according to eGFR, with stage 3 further subdivided into 3a and 3b. Treatment-related information and enrollment in pre-dialysis programs were also documented.

Quality of Life Assessment

QoL was assessed using the Romanian-validated KDQOL-36™, which comprises the SF-12 components (PCS and MCS) and three kidney-specific scales: Symptoms/Problems, Effects of Kidney Disease, and Burden of Kidney Disease.

Scores range from 0 to 100, with higher scores indicating better QoL. The questionnaire was self-administered or interviewer-administered, as appropriate. Standard scoring algorithms were used to derive PCS, MCS, subscale scores, and the Kidney Disease Summary Score (KSS).

Symptom and Clinical Assessment

Beyond KDQOL items, patients were screened for common CKD symptoms (fatigue, back pain, dysuria, sleep disturbances, pruritus, edema) via interview and exam. Edema was graded as absent, peripheral, or anasarca. Anemia (Hb <12 g/dL in women and <13 g/dL in men), erythropoietin use, and hyperkalemia (serum potassium >5.0 mmol/L) were also recorded. These variables were analyzed in relation to QoL. When abnormal values were detected, laboratory measurements were verified according to routine clinical practice.

Patient Characteristics

The study included 989 pre-dialysis CKD patients across stages I–V. The mean age of the overall cohort was 58.3 ± 12.5 years. When stratified by sex, the mean age was 58.7 ± 12.2 years in women and 56.1 ± 14.2 years in men. The median age was 62.0 years (IQR 14.0) in women and 60.0 years (IQR 20.3) in men. Age distribution differed significantly between the sexes ($p = 0.014$). The distribution by CKD stage was as follows: stage I, 18.2%; stage II, 25.3%; stage IIIa, 22.0%; stage IIIb, 15.5%; stage IV, 11.6%; and stage V, 7.4%. Sex distribution was similar across stages ($p = 0.18$), although men were slightly overrepresented in stage V (57%).

The primary CKD etiologies were chronic interstitial nephropathies (~60%), glomerulonephritis (~36%), and diabetic kidney disease (28.9%), often in association with other causes. Comorbidities were common: hypertension was present in 92.5% of patients, with no significant difference between the sexes; diabetes in 29.4%; ischemic heart disease in 9.0% (10.1% in men vs 7.6% in women, $p = 0.2$); obesity in 19.5%; and dyslipidemia in 41.2%, with a significantly higher prevalence in women than in men (48.8% vs 33.3%, $p < 0.001$). Mean eGFR was 60.1 ± 35 mL/min/1.73 m^2 and was slightly lower in men than in women (57.5 vs 66.1), consistent with the stage distribution. Median CKD duration was 4.8 years (IQR 2–8). Renal anemia was present in 54.0% of patients and was more common in women than in men (57.7% vs 48.9%, $p = 0.011$). Median hemoglobin was 123 g/L in women and 131 g/L in men. Serum albumin <35 g/L was observed in 46.8% of patients, with no significant sex difference, suggesting inflammation or malnutrition. Hyperkalemia (K^+ >5.0 mmol/L) was present in 61.9% and was more frequent in men than in women (67.3% vs 57.3%, $p = 0.003$). Overall, 86.5% of patients had at least one CKD-related complication upon evaluation.

Statistical Analysis

Statistical analyses were performed using SPSS version 23.0 and R. Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed variables are presented as mean ± standard deviation and were compared using Student's t-test or one-way analysis of variance (ANOVA), as appropriate. Non-normally distributed variables are presented as median and interquartile range (IQR) and were compared using the Mann-Whitney U test or the Kruskal-Wallis test. To capture clinically meaningful impairment, Low QoL was defined as a PCS score below the 25th percentile of the cohort. This data-driven, quartile-based threshold is consistent with established approaches in HRQoL research to identify patients at the highest risk of functional limitation.

Categorical variables are presented as absolute numbers and percentages and were compared using the chi-square test or Fisher's exact test, as appropriate. Associations between continuous clinical variables and quality-of-life scores were assessed using Pearson's or Spearman's correlation coefficients, depending on data distribution. Multivariate logistic regression analysis was used to identify independent predictors of low quality of life, defined as a Physical Component Summary (PCS) score below the 25th percentile. Variables with $p < 0.10$ in univariate analysis, together with clinically relevant covariates (age, sex, CKD stage, anemia, diabetes mellitus, hypoalbuminemia, and CKD duration), were entered into the multivariate model. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Across all analyses, a two-sided p-value < 0.05 was considered statistically significant. In addition to logistic regression, a multivariable linear regression model with PCS as a continuous dependent variable was also examined to assess the robustness of the observed associations.

RESULTS

Group comparisons and associations are presented according to variable distribution and predefined statistical models, as detailed in the Statistical Analysis section.

Symptom Burden

Most patients with CKD reported multiple symptoms. Chronic fatigue and low back pain were each present in 91.5% of patients, increasing alongside advancing disease stage and the presence of anemia. Dysuria was reported by 64.8% of patients, indicating that urinary symptoms were common in this cohort. Sleep disturbances, pruritus, and appetite loss were also frequently reported, particularly in advanced CKD.

Women had a significantly greater symptom burden than men. Specifically, fatigue and back pain were present in approximately 95% of women versus 85% of men ($p < 0.001$), while dysuria affected 70.8% of women compared to 52.6% of men ($p < 0.001$) (Figure 1). In contrast, the prevalence of edema was comparable between sexes (approximately 52% in both groups; $p = 0.90$), suggesting that fluid retention correlates more closely with overall disease severity than with patient sex (Table 1).

This difference is consistent with previous reports showing that women with CKD report symptoms more frequently and with greater intensity than men. Higher symptom burden was also associated with significantly lower QoL: patients reporting three or more moderate-to-severe symptoms had markedly lower physical function and vitality scores ($p<0.001$). These outcomes are consistent with international data, which demonstrate that a high symptom load in non-dialysis CKD reduces PCS and MCS scores by approximately 13 and 8 points, respectively. Consequently, these results highlight that the targeted management of fatigue, pain, and other predominant symptoms is essential to improving quality of life.

Table 1. Prevalence of self-reported symptoms among women and men

Symptom	Women (n=662) N (%)	Men (n=327) N (%)	p-value
Low back pain			<0.001
Yes	628 (94.9%)	277 (84.7%)	
No	34 (5.1%)	50 (15.3%)	
Dysuria			<0.001
Yes	469 (70.8%)	172 (52.6%)	
No	193 (29.2%)	155 (47.4%)	
Fatigue			<0.001
Yes	629 (95.0%)	278 (85.0%)	
No	33 (5.0%)	49 (15.0%)	
Edema			0.9
Yes	345 (52.1%)	168 (51.4%)	
No	317 (47.9%)	159 (48.6%)	

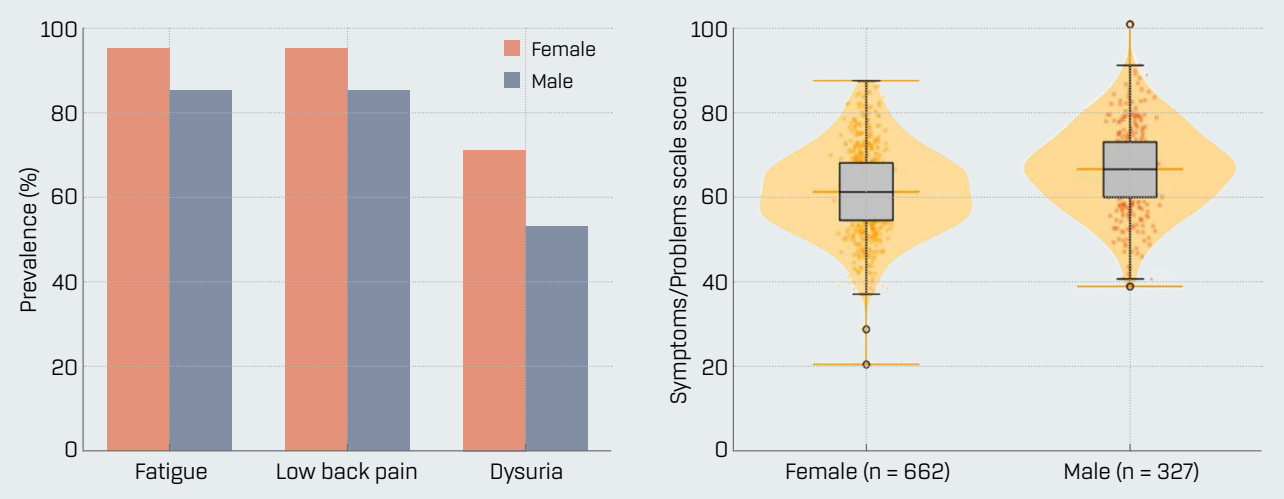

Figure 1. Prevalence of key chronic symptoms in CKD patients by gender.

Quality of Life Scores

Quality of life (QoL) was significantly impaired across the pre-dialysis CKD cohort. The mean SF-12 Physical Component Summary (PCS) and Mental Component Summary (MCS) scores were 40.2 ± 10.8 and 43.5 ± 11.2, respectively, both below the population norm of 50, indicating substantial physical and emotional impairment. Women had lower scores across all KDQOL-36 domains, including PCS (38.0 vs 41.0) and MCS (approximately 42.0 vs 45.0) ($p<0.05$). A similar pattern was observed for the kidney-specific subscales, with lower scores in women for Symptoms, Effects, and, most notably, Burden (mean 34.7 ± 21 in women vs 41.5 ± 23 in men, $p<0.01$) (Figure 2). This difference remained significant after adjustment for CKD stage, hemoglobin, and other covariates, with female sex independently associated with 3-5 point lower QoL scores.

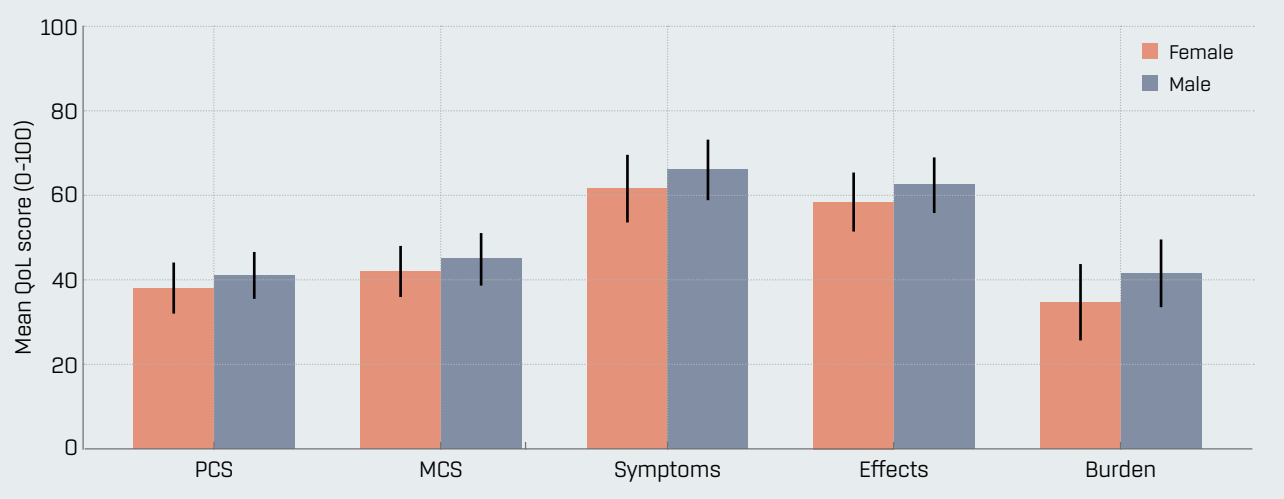

Figure 2. Health-related quality of life (HRQoL) scores in pre-dialysis CKD by gender (KDQOL-36 domains). This chart compares female (red) and male (blue) patients' mean scores (0–100 scale) on the SF-12 Physical Component (PCS) and Mental Component (MCS), and the kidney-disease-specific subscales: Symptoms/Problems, Effects of kidney disease, and Burden of kidney disease. Female patients scored lower in all domains. All gender differences were statistically significant ($p<0.05$). Error bars show standard deviations.

Quality of Life by CKD Stage

As expected, QoL deteriorated progressively with advancing CKD stage. There was a clear gradient: patients in early CKD (stages I-II) had the highest QoL scores, those in intermediate stage III had mid-range scores, and advanced CKD (stages IV-V) patients had the poorest QoL. For instance, mean PCS in stage I-II patients was 44.2, compared to 39.0 in stage III and only 34.5 in stage IV-V ($p<0.001$ across groups). A similar pattern was observed for MCS, although the decline was less pronounced, with mean values of approximately 46.7 in the early stages, 42.0 in stage III, and 39.0 in stages IV–V ($p<0.001$). The differences between early (I-II) and advanced (IV-V) groups were highly significant for both physical and mental components (Figure 3). When dichotomized, advanced-stage CKD (G4-G5) patients had an average PCS about 8 points lower and MCS ~7 points lower than those in mild CKD (G1-G2). In fact, stage IV-V patients' mean PCS of ~36 indicates severe functional impairment comparable to patients on dialysis or those with congestive heart failure. The stage-related trend was evident as well in the kidney-specific subscales: for example, the Symptoms/Problems score worsened from a mean ~75 in early CKD to ~60 in advanced CKD, and the Burden score dropped from ~45 in early stages to ~30 in stage V ($p<0.01$ for trend). The physical function and role limitations aspects of SF-36 showed the sharpest declines at advanced stages, reflecting accumulated disability. Interestingly, general mental health and emotional well-being scores, while lower in advanced CKD, did not drop as precipitously; some patients maintained stable mental QoL despite progression, possibly due to coping mechanisms or support systems. Nonetheless, overall HRQoL was significantly compromised by late-stage CKD, corroborating prior reports that each stepwise decline in GFR is associated with worse patient-reported outcomes.

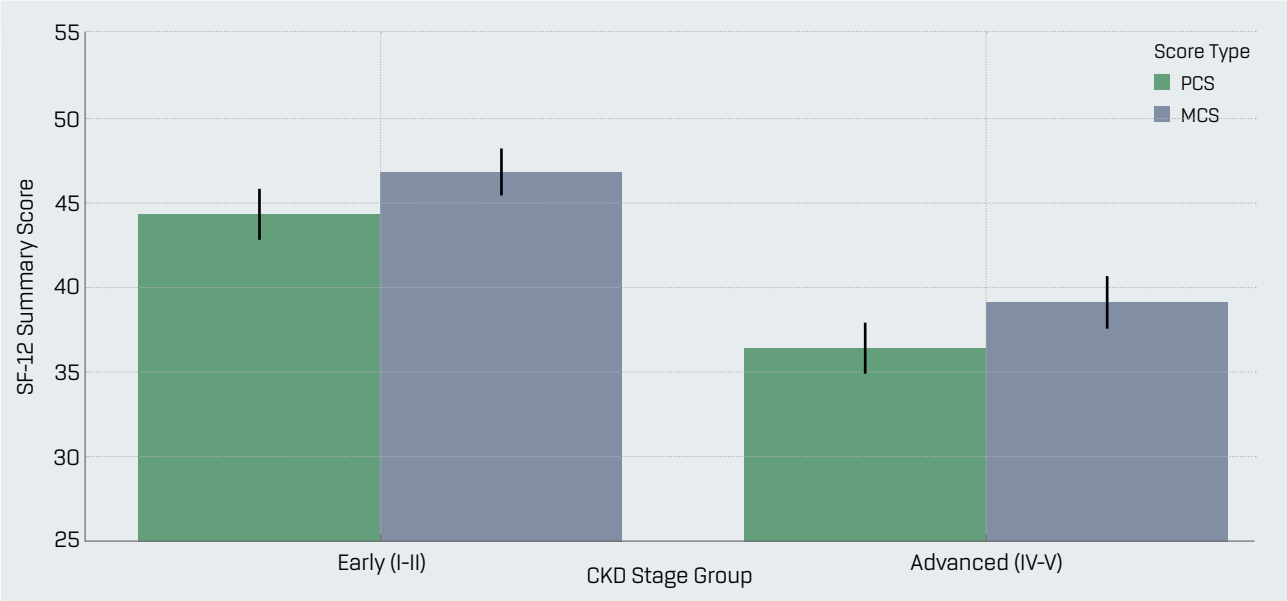

Figure 3. Physical and mental component summary scores in early vs advanced CKD stages.

Further analysis examined whether specific stage transitions were associated with the greatest impact on QoL. The largest reduction in PCS was observed between stage III and stage IV, corresponding to a decline in eGFR below ~30 ml/min; This transition is often accompanied by a substantial increase in symptom burden, including fatigue and anorexia, together with more marked lifestyle limitations. Stage V (pre-dialysis) patients had the lowest scores of all, on par with patients just starting dialysis reported in literature. Notably, there was a moderate positive correlation between eGFR and PCS ($r \approx 0.45$, $p<0.001$), indicating that better kidney function was associated with better perceived physical health. In contrast, the correlation between eGFR and MCS was weak ($r \approx 0.10$, $p=0.09$), suggesting that mental health in CKD may depend less on renal function per se than on other factors, including psychosocial support, coping mechanisms, and comorbid depression.

Factors Associated with Low QoL

Several clinical variables were strongly associated with poorer QoL. Diabetic patients had lower PCS scores by ~3.5 points and reduced kidney-specific QoL ($p<0.01$), likely due to added burdens such as neuropathy and cardiovascular disease. Similarly, patients with cardiac disease had PCS scores ~4 points lower ($p=0.02$). Anemia (Hb <11 g/dL) was linked to ~5-point lower PCS and reduced vitality ($p<0.001$), with hemoglobin moderately correlating with the Vitality subscale ($r \approx 0.5$). Hypoalbuminemia (<35 g/L) was associated with more severe symptoms ($r \approx -0.4$) and lower MCS ($r \approx -0.25$). Longer CKD duration (>5 years) was also linked to diminished social and mental functioning ($p<0.05$), possibly due to cumulative disease burden. Multivariate regression identified independent predictors of low QoL (PCS <33): advanced CKD stage (OR 2.72, 95% CI 1.9-3.9, $p<0.001$), diabetes (OR 1.94), anemia (OR 1.8), hypoalbuminemia (OR 1.7), disease duration >5 years (OR 1.5), and female sex (OR 1.38). Age >60 was not independently predictive.

DISCUSSION

This study assessed health-related quality of life in a large cohort of pre-dialysis CKD patients and examined the associations of sex, CKD stage, symptoms, and comorbidities with QoL outcomes. To current knowledge, it represents one of the most comprehensive evaluations of QoL across all stages of CKD in an Eastern European population. The present findings highlight important determinants of patient well-being in CKD and have relevant implications for nephrology practice. Given the cross-sectional design, the observed relationships should be interpreted as associative rather than causal.

Quality of Life in CKD – Overall Impact

The present findings confirm that CKD has a substantial adverse effect on quality of life even before the onset of dialysis. Mean PCS and MCS scores in this pre-dialysis cohort were markedly lower than population norms, indicating significant impairment in both physical and mental health. The reduction in physical QoL, with a mean PCS of approximately 40, is comparable to that reported in patients with advanced heart failure or COPD, highlighting the considerable burden of CKD. This observation is consistent with previous studies showing that HRQoL is significantly reduced in CKD and declines further as kidney function worsens (6). Even in stage III CKD, often considered mild to moderate, patients showed meaningful limitations in energy and physical functioning, indicating that CKD may affect daily life well before the onset of kidney failure (12). The progressive decline in QoL with advancing CKD stage is also consistent with previous cross-sectional studies (13). In particular, patients in stages IV–V had PCS and MCS scores approximately 7–8 points lower than those in stages I–II, confirming a statistically and clinically significant decline. Each 10 mL/min drop in eGFR roughly corresponded to a few-point drop in PCS in our cohort. Importantly, mental QoL did not decline as steeply as physical QoL, as reported in other studies (14). This pattern may reflect a degree of psychological adaptation or resilience; however, by stage V, even mental health scores were quite low (~39). These findings further indicate that QoL impairment in CKD is multidimensional. In addition to the generic SF-12 components, the kidney-specific domains of the KDQOL-36—Symptoms, Effects, and Burden—captured important aspects of symptom distress and illness intrusiveness. The Burden of Kidney Disease domain, in particular, showed very low mean scores, reflecting the extent to which CKD affects daily life through dietary restrictions, medication burden, and concern about future disease progression. Taken together, these findings highlight the importance of addressing not only biomedical targets, but also the functional and psychological burden of CKD in routine clinical care (15).

Gender Disparities

A notable finding of this study was the clear difference in QoL between female and male patients with CKD. Female patients consistently reported poorer QoL than male patients across all five KDQOL-36 subscales, despite having, on average, slightly less advanced disease according to some clinical measures, including eGFR. After adjustment for CKD stage and comorbidities, female sex remained an independent predictor of low QoL (OR ~1.4). This finding is consistent with reports from other CKD cohorts and chronic disease populations. Fletcher et al. (6), for example, showed that women with CKD often experience a greater symptom burden and poorer HRQoL, a pattern observed across different settings. In the present cohort, women reported significantly higher rates of fatigue, pain, and urinary symptoms than men, which may partly explain their lower QoL scores. The literature suggests several reasons for this gender gap: biologically, women might experience certain symptoms more intensely (e.g. higher prevalence of anemia-related fatigue, as we saw, and greater likelihood of UTI-related discomfort) (16). Psychosocial factors

may also contribute, as women may be more likely to report symptoms and emotional distress, whereas men may underreport symptoms or use different coping strategies. In addition, women with chronic illness often face distinct social roles and responsibilities, including caregiving demands, which may increase the perceived burden of disease. The present data showed women had especially low scores on the Burden scale, indicating they felt more encumbered by the illness in daily life (17). This could be due to role expectations; for instance, dietary restrictions and functional limitations related to CKD may interfere more substantially with family and daily responsibilities or coincide with lower levels of social support.

Interestingly, despite poorer QoL among women, epidemiological data indicate that men are more likely to progress to ESRD more rapidly (7). This paradox has been described previously: although CKD progression tends to be slower in women, this may coexist with poorer perceived health, possibly because of a greater symptom burden or disparities in access to care (18). In an international CKD outcomes study (CKDopps), women with non-dialysis CKD were more likely than men to report a high symptom burden (adjusted OR ~1.5), which was associated with lower physical QoL. Similar findings have been reported in dialysis populations, where women have also been shown to have poorer QoL and higher rates of depression than men (19).

These findings support the need for a gender-sensitive approach to CKD management. Symptoms and QoL should be assessed routinely, particularly in female patients, in whom symptom burden may be greater. Targeted treatment of anemia, appropriate pain management, and psychosocial support may be especially important for improving QoL in this group. Multidisciplinary care involving dietitians, social workers, and psychologists may also help address the broader challenges associated with living with CKD (20). Although interventional outcomes were not examined directly in this study, female sex emerged as a marker of greater symptom burden and poorer QoL, supporting the need for proactive supportive care.

Symptom burden and comorbidities

Beyond gender and CKD stage, symptom burden and comorbidities appeared to be major determinants of QoL in this present study. Fatigue, pain, and related symptoms are not merely consequences of CKD, but important contributors to impaired functioning and reduced well-being (6). Fatigue, reported by 91% of patients, was strongly associated with lower vitality and poorer physical QoL scores. This is consistent with the findings of Farag et al. (2023), who showed that anemia-related fatigue in CKD significantly impairs physical activity (21). Treatment of anemia remains one of the few interventions shown to improve QoL in CKD, in line with trial data indicating that modest increases in hemoglobin may lead to better energy levels and physical functioning. In this cohort, each 1 g/dL decrease in hemoglobin was associated with a meaningful decline in PCS and vitality scores, supporting the importance of appropriate anemia management as a QoL-oriented strategy (21).

Pain also appears to be an under-recognized determinant of reduced QoL in CKD. Nearly 92% of patients reported chronic back pain, and pain is known to adversely affect sleep and mental health. Adequate analgesia, with careful attention to renal dosing, together with treatment of renal bone disease or neuropathy when present, may help improve patients' daily comfort and QoL (22). Comorbidities such as diabetes were identified as independent predictors of poor QoL. Diabetic CKD patients are likely to experience multiple contributors to symptom burden, including neuropathy, vascular complications, and dietary restrictions, which may further worsen quality of life. Previous studies have likewise shown that diabetes is associated with poorer physical QoL

and higher rates of hospitalization. These findings are consistent with other reports (23), which have shown that comorbid chronic conditions, particularly depression and diabetes, synergistically lower QoL in older adults. Ischemic heart disease and heart failure were also more common in the studied men and were associated with lower QoL, though the effect size was smaller after controlling for stage and anemia. Given that cardiovascular disease remains a leading cause of death in CKD, its presence may also signal a reduced exercise capacity and more hospital visits, affecting QoL (24).). Together, these findings underscore the importance of optimal management of comorbid conditions in CKD. Cardiovascular risk reduction, glycemic control, and appropriate treatment of complications may help preserve or improve QoL, in addition to improving survival.

Another notable finding was that hypoalbuminemia was associated with lower QoL, particularly with greater symptom burden and poorer mental health. Serum albumin is a marker of nutritional and inflammatory status, and reduced albumin levels in CKD often accompanies anorexia, inflammation, and muscle wasting – all factors that can make patients feel unwell (25). We found patients with albumin <35 g/L had more severe symptom scores ($r = -0.4$). This observation is consistent with the malnutrition-inflammation complex described in CKD, which has been linked to fatigue, frailty, and depression. Nutritional support and anti-inflammatory strategies may therefore contribute indirectly to improved QoL by raising albumin or reducing inflammation, although this remains challenging in clinical practice. Nonetheless, recognizing a low albumin as a red flag for poor QoL could prompt clinicians to involve dietitians or start an early oral nutrition support.

Limitations

Several limitations should be considered when interpreting these findings. The cross-sectional design did not allow assessment of changes in QoL over time and precluded any inference of causality. Data were based on patient self-report and medical records and were therefore subject to potential reporting bias, although validated tools were used. The inclusion of a single-country, ethnically homogeneous cohort may also limit the generalizability of the results. In addition, depression and anxiety were not evaluated using standardized psychometric instruments, such as the PHQ-9 or HADS, and their contribution to impaired mental QoL may therefore have been underestimated. Other potentially relevant clinical variables, including comorbidity severity and treatment adherence, were not fully detailed. Despite these limitations, the large sample size and robust methodology of the study support the overall reliability of the findings.

CONCLUSIONS

1. This study demonstrates that quality of life (QoL) was substantially impaired in patients with CKD prior to dialysis, particularly among women and those with advanced stages (G4-G5). These groups reported lower physical and mental health scores and a greater symptom burden.
2. Diabetes, anemia, hypoalbuminemia, and longer disease duration were independently associated with poorer QoL, indicating that these factors represent important targets for clinical intervention.
3. Routine assessment of QoL should be incorporated into the care of patients with CKD, together with a multidisciplinary approach focused on medical management, symptom control, and psychosocial support.

4. Tailored interventions, especially for high-risk patients (e.g., female sex, CKD stages IV–V, presence of diabetes or anemia), may improve daily functioning and overall well-being.
5. From a public health perspective, both slowing CKD progression and addressing the patient experience should be considered core priorities, as QoL emerges as a critical patient-reported outcome for clinical decision-making and the development of more holistic care models for individuals with CKD.

CONFLICT OF INTEREST

The author declares no conflicts of interest related to this work. The research was conducted independently and received no industry funding.

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ETHICAL APPROVAL

The study protocol was approved by the Ethics Committee of the Nicolae Testemițanu State University of Medicine and Pharmacy, Chișinău (Approval No. 35, issued April 2023). All participants provided written informed consent. The study was conducted in accordance with the Helsinki Declaration and applicable national regulations for research in human subjects, with particular care to protect patient confidentiality and well-being. No experimental interventions were performed; only questionnaire and observational data were collected. Participants identified with severe depressive symptoms or distress during interviews were offered referral to counseling services as an ethical measure to ensure their well-being.

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