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ORIGINAL PAPER

CHRONIC KIDNEY DISEASE AND HEALTH-RELATED QUALITY OF LIFE IN REPUBLIC OF MOLDOVA

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Abstract

Introduction. Chronic kidney disease (CKD) significantly affects patients' health-related quality of life (HRQoL), especially in the advanced stages.
The objective of the study. This study aimed to assess HRQoL among CKD patients (stages 1-5, non-dialysis) in the Republic of Moldova using the KDQOL-SF questionnaire, and to analyse the relationship between quality of life, clinical-biochemical parameters, sociodemographic variables, and disease stage.
Material and methods. A cross-sectional study was conducted on a cohort of patients diagnosed with CKD stages 1–5, who were not receiving dialysis. HRQoL was evaluated using the KDQOL-SF, which includes both generic (SF-36) and kidney disease-specific domains. Clinical (e.g., diabetes, hypertension), biochemical (e.g., creatinine, urea, hemoglobin, albumin),

Résumé

La maladie rénale chronique et la qualité de vie liée à la santé en République de Moldova

Introduction. L'insuffisance rénale chronique (IRC) a un impact significatif sur la qualité de vie liée à la santé (QVLS) des patients, en particulier aux stades avancés.
L'objectif de l'étude. Cette étude visait à évaluer la QVL chez les patients atteints d'IRC (stades 1 à 5, non dialysés) en République de Moldova à l'aide du questionnaire KDQOL-SF, et à analyser la relation entre la qualité de vie, les paramètres cliniques et biochimiques, les variables sociodémographiques et le stade de la maladie.
Matériel et méthodes. Une étude transversale a été menée auprès d'une cohorte de patients chez lesquels une insuffisance rénale chronique (IRC) de stade 1 à

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and socio-demographic data were collected and analysed in relation to disease stage and HRQoL scores.
Results. HRQoL scores decreased progressively with CKD severity, with the most pronounced declines in physical function, vitality, and symptom burden. Women consistently reported lower scores than males across all dimensions. Advanced CKD stages were significantly associated with higher creatinine and urea levels, lower hemoglobin and albumin, older age, lower income, unemployment, and presence of comorbidities. An inconsistent slight improvement in HRQoL scores in stage 5 was observed, possibly due to psychological adaptation and survival bias.
Conclusions. The study highlights a clear association between CKD progression and declining HRQoL, particularly in physical and psychosocial domains. Gender disparities and socioeconomic inequalities further compound the impact. These findings underscore the need for personalized, multidisciplinary care strategies that integrate HRQoL monitoring, early detection, risk factor control, and targeted support for vulnerable groups. Integrating HRQoL assessment into routine clinical care could enhance patient-centred outcomes in CKD management.

Keywords: chronic kidney disease, health-related quality of life, socio-demographic factors, biochemical markers.

List of abbreviations:
CKD – chronic kidney disease
HRQoL – health-related quality of life
KDQOL-SF – kidney disease quality of life – Short Form
GFR – glomerular filtration rate
KDIGO – kidney disease: improving global outcomes
GBD – global burden of disease
QoL- quality of life

5 avait été diagnostiquée et qui ne suivaient pas de dialyse. La qualité de vie liée à la santé (HRQoL) a été évaluée à l'aide du questionnaire KDQOL-SF, qui comprend à la fois des domaines génériques (SF-36) et des domaines spécifiques à la maladie rénale. Des données cliniques (par exemple, diabète, hypertension), biochimiques (par exemple, créatinine, urée, hémoglobine, albumine) et sociodémographiques ont été recueillies et analysées en fonction du stade de la maladie et des scores de QVLS.
Résultats. Les scores de qualité de vie liée à la santé (HRQoL) ont diminué progressivement avec la gravité de l'IRC, les baisses les plus marquées concernant la fonction physique, la vitalité et la charge symptomatique. Les patientes ont systématiquement rapporté des scores inférieurs à ceux des patients masculins dans toutes les dimensions. Les stades avancés de l'IRC étaient significativement associés à des taux plus élevés de créatinine et d'urée, à des taux plus faibles d'hémoglobine et d'albumine, à un âge plus avancé, à des revenus plus faibles, au chômage et à la présence de comorbidités. Une légère amélioration incohérente des scores de QVLS au stade 5 a été observée, peut-être due à une adaptation psychologique et à un biais de survie.
Conclusions. Cette étude met en évidence un lien manifeste entre la progression de l'IRC et la détérioration de la QVLS, en particulier dans les domaines physique et psychosocial. Les disparités entre les sexes et les inégalités socio-économiques aggravent encore cet impact. Ces résultats soulignent la nécessité de mettre en place des stratégies de soins personnalisées et multidisciplinaires intégrant le suivi de la QVLS, le dépistage précoce, la maîtrise des facteurs de risque et un soutien ciblé aux groupes vulnérables. L'intégration de l'évaluation de la QVLS dans les soins cliniques courants pourrait améliorer les résultats centrés sur le patient dans la prise en charge de l'IRC.

Mots-clés: insuffisance rénale chronique, qualité de vie liée à la santé, facteurs sociodémographiques, marqueurs biochimiques.

Introduction

Chronic kidney disease (CKD) is characterized by a slow and progressive decline in kidney function over a period of months or years, which may progress to end-stage renal disease, requiring renal replacement interventions such as dialysis or transplantation. Diagnosis is generally based on the presence of a persistent low glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2, or the identification of specific markers of renal impairment (microalbuminuria, haematuria) that persist for a minimum duration of three months[1]. CKD has a slow progression and often lacks overt clinical manifestations in the early stages, with most patients being diagnosed only when renal function falls below 30 mL/min/1.73 m^2. According to the Kidney Disease Global Outcomes Improvement Initiative (KDIGO), CKD is recognized as a genuine public health problem on a global scale. This characterization underscores the need for a concerted global approach to prevention, early detection and effective disease management[2].

CKD has become one of the major concerns of health systems globally because of its increasing

prevalence and debilitating effects on patients. In 2017, the total number of people affected by CKD in all stages was estimated at nearly 697.5 million, representing approximately 9.1% of the global population[2]. Compared to 1990 data, this reflects an increase of more than 29% among all age groups. CKD-related mortality experienced an alarming rise: more than 1.2 million deaths recorded in 2017, equivalent to a 41.5% increase since 1990[2].

Related to human costs, CKD generates a major economic impact on public health budgets. In the United States of America in 2021, people aged 65 and over with a diagnosis of CKD accounted for 13.5% of Medicare beneficiaries, but contributed nearly a quarter of total Medicare spending – about 76.8 billion dollars[1]. Caring for patients with CKD has become increasingly costly, with more than 40% increase in spending between 2011-2021[1]. In China, the financial burden of this disease is estimated to reach 198 billion dollars in 2025, up from 179 billion dollars in 2019[2].

CKD generates important indirect effects to the direct costs of health care systems, such as decreased productivity, degraded quality of life, limited work capacity, and a significant emotional burden on patients and their families. Because this widespread influence on public health and the economy, the World Health Organization has included CKD in the list of global priorities as part of the Global Burden of Disease (GBD) assessment[3].

Quality of life (QoL) has become an essential benchmark and a central component in the assessment of patients' health status, both in clinical research and in current medical practice. In the past, attention has been predominantly focused on traditional biomedical indicators without considering subjective dimensions of well-being[3]. However, in recent decades, there has been a paradigm shift, reflected by a growing interest in the impact of diseases and treatments on patients' daily lives. Thus, QoL assessment tools are increasingly being integrated into clinical trials and medical management strategies. HR in relation to health status provides a complex picture of how factors such as socio-economic status, living environment, spiritual beliefs and support network influence self-perceptions[4]. These determinants play an essential role in clinical decisions and in personalizing therapeutic strategies, providing a holistic view of the patient's well-being[5].

Patients' QoL expresses in a complex way their level of physical, psychological and social well-being, reflecting their ability to carry out activities of daily living and cope with the demands of everyday life[5]. This includes not only the absence of illness, but also the individuals' subjective perception of their general health, energy levels, interpersonal relationships and social functioning. Thus, QoL is an essential indicator in assessing the impact of chronic diseases, such as chronic kidney disease, on patients' lives[6].

People diagnosed with CKD often experience various difficulties that affect their physical functioning, emotional state and ability to interact socially. These difficulties lead to a reduced overall QoL[6]. In fact, this decrease in QoL is considered one of the most serious challenges faced by patients with CKD, with the potential to negatively influence the course of the disease over time[7]. Furthermore, the impact of the disease on the patient differs depending on the stage of the disease. In the early stages, patients may experience a lesser impact, whereas as the disease progresses and nears renal failure, the burden of the disease becomes more pronounced. This translates into significant reductions in health-related quality of life (HRQoL), as well as decreased life expectancy[8]. On a global scale, the integration of HRQoL indicators into the clinical management of patients with CKD has gained increasing importance. This is due to numerous studies that have shown a significant correlation between low levels of HRQoL and increased risks of morbidity and mortality among these patients[9]. Thus, monitoring and assessment of HRQoL become essential components in the therapeutic approach, contributing to optimize clinical outcomes and improve patient prognosis[10].

Although much research has focused on the assessment of QoL in patients with CKD undergoing hemodialysis, information on QoL status in patients receiving conservative treatment for this condition remains limited. There is also a lack of in-depth data on how QoL changes in the early stages of the disease. The available studies indicate that patients on conservative treatment have a lower QoL compared to the general population, but it is still higher than that reported by patients on hemodialysis treatment[10]. Certain clinical aspects, such as the presence of anemia, comorbidities and early initiation of medical management by a nephrology specialist, seem to play an important role in determining the level of QoL in these patients[11]. To date, no systematic assessment of HRQoL among patients with CKD in the Republic of Moldova not receiving renal replacement therapy (RRT) was conducted. This omission has led to a significant underestimation of the total burden of CKD in this vulnerable population. A significant gap remains in the literature regarding the impact of CKD on patients' QoL, particularly in the Republic of Moldova. Further research is needed to support the development of tailored clinical strategies and health policies aimed at improving patient outcomes and QoL.

In-depth knowledge of HRQoL among this group is essential as it provides important insights into the challenges and needs faced by people at various

stages of CKD. By identifying and understanding the socio-demographic and clinical factors that have a significant impact on HRQoL in patients with CKD, health professionals can more effectively tailor and personalize treatment plans and therapeutic interventions. This individualized approach is essential to adequately address the unique needs of each patient, thereby helping to improve their overall health and delay disease progression. Moreover, the data collected through HRQoL assessments can serve as a basis for public health policymaking and the development of more targeted health intervention strategies to ensure effective and tailored support for patients with CKD, both at the local community level and in primary care settings. Thus, integrating this information into medical practice may lead to more comprehensive and effective management of CKD in the affected population. Using the standardized KDQoL™-36 instrument, this study will conduct a comprehensive assessment of HRQoL in patients with CKD, focusing on three major dimensions: physical, mental, and specific aspects of kidney health. This research is particularly relevant in a resource-limited setting where such data are extremely scarce and under-documented. Unlike most previous studies, which have been conducted in high-income countries with well-developed health systems, this investigation provides important insights into the QoL of patients from an economically disadvantaged background, contributing to a deeper understanding of the specific challenges faced by this population. In addition, the study will analyze in detail the correlations between HRQoL and several socio-demographic (such as age, gender), clinical (including disease stage, presence of primary kidney disease and presence of comorbidities) and laboratory factors. This research will serve as a foundation for future studies, providing essential information that can guide the development and implementation of specific strategies and interventions aimed at reducing the burden of CKD and significantly improving the QoL of patients living in resource-limited settings.

Therefore, the aim of this study is to assess a little investigated area of HRQoL in patients with CKD not receiving RRT in the Republic of Moldova. Given the socio-economic specificities and challenges of the health care system in this low-income country, this research aims to make an important contribution to understanding and improving the clinical management of this vulnerable category of patients. The analysis was conducted on a large and representative sample of adults in the Republic of Moldova, aged between 18 and 79 years.

The objective of the study was to assess the HRQoL across the full spectrum of non-dialysis dependent CKD (stages 1–5) and to determine the impact of clinical, biochemical, and socio-demographic factors on patients' well-being.

Materials and methods

Study design and subject

This cross-sectional study was carried out in the Nephrology Department of IMSP Timofei Mosneaga Republican Clinical Hospital, recognized as a national reference center and the most important tertiary hospital in the Republic of Moldova, between 2022-2023. The study was conducted in accordance with the ethical standards of the institutional and national research committees and the Helsinki Declaration. All participants provided written informed consent prior to their inclusion in the study. The research included patients diagnosed with CKD, in all evolution stages, who were not receiving RRT. The institution provides advanced care services to a heterogeneous population from urban and rural areas, with varying socio-economic profiles and with different degrees of severity of CKD. Given this diversity, the study sample can be considered representative of the national population affected by CKD, which contributes to the increased relevance and applicability of the results obtained.

Inclusion criteria:

- age ≥18 years;
- confirmed diagnosis of CKD, and
- informed consent expressed by signing the participation agreement.

Exclusion criteria:

- patients undergoing hemodialysis or undergoing renal transplantation;
- under 18 years of age or over 80 years of age;
- patients with acute kidney injury, oncologic diseases;
- patients who refused participation;
- insufficient educational level to independently complete the questionnaires used in the study.

The study participants completed the revised version of the *Kidney Disease Quality of Life – Short Form* (KDQOL-SF™ v1.3), a validated tool for assessing QoL specific to patients with CKD[12]. This instrument was administered in its Romanian version, which has been formally translated and cross-culturally adapted for use in the Republic of Moldova to ensure its clinical relevance and psychometric reliability. The questionnaire was used to assess physical, psychological and disease impact dimensions of daily life. Relevant clinical and paraclinical data were collected both through structured interviews with patients and retrospective analysis of the existing medical records in the electronic files, using the hospital's internal computer

system "HIPOCRATE" (Hyper Text Transfer Protocol with Privacy). This combined approach allowed a comprehensive assessment of the clinical profile and QoL of the patients included in the study.

This study was approved by the Ethical Committee of Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova (approval no. 35 of April 25, 2023). All participants provided written informed consent prior to enrolment. The patient's personal identification and information were codified before it was used for research. The authors confirmed that all experiments were performed in accordance with relevant guidelines and regulations.

Sample size calculation

The sample size for this cross-sectional study was estimated using a combined approach, applying both the recommendations for multivariate regression models and classical statistical formulae for comparisons between means and proportions, as follows:

- multivariate regression-based estimation: 450 patients.

In multivariate analysis, a minimum of 10-15 subjects is recommended for each explanatory variable included in the model. Considering 15 main variables (including stage of CKD, age, sex, disease duration, comorbidities, etc.), the minimum required size was estimated at 225 patients (15×15). To compensate for an estimated non-participation or data loss rate of approximately 15%, the adjusted size was approximately 265 patients. Given the intention to perform subgroup analyses and to increase statistical power, the sample was expanded to 450 patients.

- estimation for comparison of two means: 196 patients; adjusted for 15% losses: 231 patients.
- estimate for comparing two proportions: 95 per group, total of 190 patients; adjusted for losses: 224 patients.

Given the complex objectives of the study, the number of variables included and the need for high analytical robustness, it was decided to include a large sample of 989 patients (662 women and 327 men), consecutively selected from among the eligible patients who presented for follow-up during the study period. This non-probability convenience sampling reflects the diversity of patients with CKD from urban and rural settings, covering all stages of the disease and different socioeconomic levels. This approach ensures good representativeness and generalizability of the results at the national level.

Stages of CKD

For all study participants, renal function was estimated based on the eGFR, calculated by the CKD-EPI 2021 formula[13], according to current international guidelines in nephrology. CKD stages were categorized according to the estimated eGFR level expressed in mL/min/1.73 m^2:

- stage 1: eGFR≥90 mL/min/1.73 m^2;
- stage 2: eGFR≥60-89 mL/min/1.73 m^2;
- stage 3: stage 3a: eGFR≥30-44 mL/min/1.73 m^2; stage 3b: eGFR≥45-59 mL/min/1.73 m^2;
- stage 4: eGFR≥15-29 mL/min/1.73 m^2;
- stage 5: eGFR<15 mL/min/1.73 m^2.

To facilitate statistical analysis and interpretation of results according to disease severity, these stages were subsequently aggregated into three synthetic categories:

- early stage: patients in stages 1 and 2;
- moderate stage: patients falling into stages 3a and 3b;
- advanced stage: patients with eGFR corresponding to stages 4 and 5 (in the absence of RRT).

This approach allowed a more efficient comparative assessment of QoL scores and other clinical parameters according to the degree of renal function impairment.

Data collection tools

Between February 2022 and February 2023, face-to-face interviews were conducted with a total of 1,235 patients diagnosed with CKD, hospitalized in the Nephrology Department of IMSP Timofei Mosneaga Republican Clinical Hospital, Chisinau. After applying inclusion and exclusion criteria, 989 eligible participants were finally selected for analysis. The interviews were conducted in a private setting, by specialist physicians and residents of the ward, using a structured questionnaire that covered socio-demographic information (age, sex, educational level, income), clinical parameters and the standardized component of quality-of-life assessment for patients with kidney disease – KDQoL™-36. Completion of the questionnaire took approximately 20-30 min in each patient.

Clinical data were obtained by standardized methods extracted from the patients' medical records. These included laboratory values collected during hospitalization (hemoglobin, serum creatinine, urea, uric acid, electrolytes, proteinuria), as well as relevant medical history (presence of diabetes mellitus, hypertension, cardiovascular disease). Primary causes of kidney disease were also identified, including tubulo-interstitial nephropathy, renal lithiasis, glomerulopathies, hereditary conditions (such as autosomal dominant polycystic kidney disease), diabetes mellitus and hypertension. Body mass index (BMI) was calculated as the ratio of weight (kg)/height^2 (m^2), and patients were classified into four categories according to World Health Organization guidelines: underweight (BMI≤18.5 kg/m^2), normal weight (BMI

18.5-24.9 kg/m^2), overweight (BMI 25.0-29.9 kg/m^2) and obese (BMI≥30 kg/m^2) [WHO Consultation, 2000]. The participants were informed in advance about the purpose and conduct of the study, and inclusion in the research was only achieved after signing written informed consent.

For the assessment of QoL in patients with CKD, version 1.3 of the KDQOL-SF™ questionnaire, validated in Romanian[14] was used. This instrument was chosen due to its superior sensitivity and specificity in capturing the impact of kidney disease on the physical, psychosocial and functional dimensions of the patient's life compared to other generic questionnaires for assessing QoL in the context of chronic disease. The structure of the KDQOL-36™ questionnaire combines a general component, taken from the Short Form-12 (SF-12), with one specific to CKD, totaling 36 items. The two subscales derived from the SF-12, the Physical Component Summary (PCS) and the Mental Component Summary (MCS), assess the perception of general physical and mental health. To these are added three dimensions specific to kidney disease: Symptoms and Problems of Kidney Disease (SPKD), Effects of Kidney Disease (EKD), and the perceived Burden of Kidney Disease (BKD). The patients's responses are transformed into standardized scores, ranging from 0 to 100, where higher values reflect a perceived better QoL. The KDQOL-36 Kidney Disease Summary Score (KSS), which aggregates the SPKD, EKD and BKD dimension scores into a single composite index, easily comparable between groups or in longitudinal analysis, was also used to provide a summary picture of the impact of kidney disease[15]. The official algorithm available in the Excel file provided by the RAND Corporation, which can be downloaded free of charge from https://www.rand.org/health/surveys_tools/kdqol.html, was used for scoring. Given that our study included only patients with CKD in pre-dialysis stages, questions 23 and 24 (which refer to hemodialysis treatment) were removed from the application to accurately reflect the characteristics of the cohort under investigation.

Statistical analysis of the data

Statistical processing was performed using the IBM SPSS version 25 package (IBM Corp., Armonk, NY), and Stata 16 software (StataCorp, College Station, TX) was used for further analysis, allowing independent validation of the results obtained. For quantitative variables, the data were summarized by central tendency and dispersion indicators: arithmetic mean ± standard deviation for normal distributions and median and interquartile range (IQR) for non-normal distributions. Qualitative variables were presented as absolute frequencies and percentages. The distribution of patients was analyzed according to the stages of CKD, age, sex and presence of comorbidities. Comparisons between two groups (e.g. QoL scores between men and women) were performed by independent samples t-test, after checking for homogeneity of variances (Levene's test) and normality of distribution. For comparisons between three or more groups (e.g. between stages 1-5 of CKD), one-way analysis of variance (ANOVA) was applied, followed by post-hoc tests (Bonferroni or Tukey) where differences were significant. Associations between categorical variables (such as stage of disease and presence of hypertension) were tested using the chi-square (χ^2) test, assessing whether proportions differed significantly between groups (e.g. patients in early versus advanced stages of CKD). For the analysis of relationships between continuous variables, the Pearson correlation coefficient was used when the distribution of both variables was approximately normal; otherwise, the Spearman coefficient was used. These correlations included analyzing the relationship between QoL scores (PCS – physical component, MCS – mental component, and KSS – renal summary score) and variables such as age, disease duration, hemoglobin values, serum creatinine or other laboratory data. To identify independent factors associated with QoL and to control for the potential influence of confounding variables, binary logistic regression and multiple linear regression models were developed. The linear regression models allowed the assessment of the impact of each predictor on continuous QoL scores (PCS, MCS, KSS). For example, the model with the KSS score as the dependent variable indicated that disease stage, age and occupational status (employed vs. not employed) significantly influenced the perceived level of kidney disease-related QoL. Thus, patients with advanced stages of CKD, the elderly, and those not employed (retired, unemployed) reported lower KSS scores, even after adjusting for the other factors included in the model. All statistical analyses were interpreted at a significance level of $p<0.05$.

Results

Socio-demographic distribution of people with CKD

The study included a total of 989 patients, distributed into five stages of chronic kidney disease (CKD) as follows: stage 1 – 307 patients (31.0%), stage 2 – 258 (26.1%), stage 3 – 195 (19.7%), stage 4 – 151 (15.3%) and stage 5 – 78 patients (7.9%) (Table 1).

The mean age increased progressively from stage 1 (52.8±14.7 years) to stage 3 (61.7±0.6 years), after which it decreased slightly in stages 4 (58.1±12.7) and 5 (58.4±12.5) (Table 1). Age differences between

Table 1. Demographic and clinical characteristics of people with CKD by age, marital status, and stage of CKD

Stage	1, N = 307*	95% CI**	2, N = 258*	95% CI**	3, N = 195*	95% CI**	4, N = 151*	95% CI**	5, N = 78*	95% CI**	Test Statistic	p-value***
Age	52.8 (14.7) 57.0 (22.0) 18.0 (76.0)	51.54	59.9 (11.5) 62.0 (13.0) 18.0 78.0	59.61	61.7 (10.6) 64.0 (14.0) 28.0 80.0	60.63	58.1 (12.7) 61.0 (14.0) 18.0 78.0	56.60	58.4 (12.5) 60.5 (15.5) 21.0 86.0	56.61	59	**<0.001**
Marital status											24	**0.020**
Married	284 (92.5%)	90%, 95%	231 (89.5%)	86%, 93%	164 (84.1%)	79%, 89%	131 (86.8%)	81%, 92%	67 (85.9%)	78%, 94%		
Divorced	10 (3.3%)	1.3%, 5.2%	9 (3.5%)	1.2%, 5.7%	6 (3.1%)	0.65%, 5.5%	11 (7.3%)	3.1%, 11%	3 (3.8%)	-0.42%, 8.1%		
Unmarried	1 (0.3%)	-0.31%, 0.96%	1 (0.4%)	-0.37%, 1.1%	0 (0.0%)	0.00%, 0.00%	0 (0.0%)	0.00%, 0.00%	1 (1.3%)	-1.2%, 3.8%		
Widow/ widower	12 (3.9%)	1.7%, 6.1%	17 (6.6%)	3.6%, 9.6%	25 (12.8%)	8.1%, 18%	9 (6.0%)	2.2%, 9.7%	7 (9.0%)	2.6%, 15%		

*Note: *Mean (SD); **Confidence Interval (CI); ***Kruskal-Wallis rank sum test; Pearson's Chi-squared test*

Table 2. Distribution of patients with CKD according to occupational status and disease stage

Stage	1, N = 307	95% CI**	2, N = 258*	95% CI**	3, N = 195*	95% CI**	4, N = 151*	95% CI**	5, N = 78*	95% CI**	Test Statistic	p-value***
Occupation											87	**<0.001**
Farmer	7 (2.3%)	0.61%, 3.9%	2 (0.8%)	-0.29%, 1.8%	2 (1.0%)	-0.39%, 2.4%	1 (0.7%)	-0.63%, 2.0%	1 (1.3%)	-1.2%, 3.8%		
Office	108 (35.2%)	30%, 41%	50 (19.4%)	15%, 24%	30 (15.4%)	10%, 20%	31 (20.5%)	14%, 27%	10 (12.8%)	5.4%, 20%		
Household	13 (4.2%)	2.0%, 6.5%	4 (1.6%)	0.04%, 3.1%	2 (1.0%)	-0.39%, 2.4%	2 (1.3%)	-0.50%, 3.1%	7 (9.0%)	2.6%, 15%		
Merchant	9 (2.9%)	1.0%, 4.8%	3 (1.2%)	-0.15%, 2.5%	0 (0.0%)	0.00%, 0.00%	4 (2.6%)	0.09%, 5.2%	4 (5.1%)	0.23%, 10%		
Office	1 (0.3%)	-0.31%, 0.96%	0 (0.0%)	0.00%, 0.00%	0 (0.0%)	0.00%, 0.00%	0 (0.0%)	0.00%, 0.00%	0 (0.0%)	0.00%, 0.00%		
Pension	158 (51.5%)	46%, 57%	194 (75.2%)	70%, 80%	158 (81.0%)	76%, 87%	106 (70.2%)	63%, 77%	54 (69.2%)	59%, 79%		
Daily laborer	11 (3.6%)	1.5%, 5.7%	5 (1.9%)	0.26%, 3.6%	3 (1.5%)	-0.19%, 3.3%	7 (4.6%)	1.3%, 8.0%	2 (2.6%)	-0.94%, 6.1%		

*Note: *Mean (SD); **Confidence Interval (CI); ***Kruskal-Wallis rank sum test; Pearson's Chi-squared test*

groups were statistically significant (p<0.001). Marital status analysis showed that most patients were married, with percentages ranging from 84.1% in stage 3 to 92.5% in stage 1. The proportion of widowed persons increased in later stages, reaching a maximum of 12.8% in stage 3. The differences between the groups were significant (p=0.020).

In terms of occupational status, there were clear differences between stages (p<0.001). The proportion of retired people increased with disease severity: from 51.5% in stage 1 to 81.0% in stage 3. In contrast, the proportion of those with clerical work was decreasing – from 35.2% in stage 1 to 12.8% in stage 5 (Table 2).

Household income showed an inversely proportional gradient with disease stage. In stage 1, only 27.7% of patients reported very low income, compared to 31.4% in stage 2, 33.1% in stage 4 and 28.2% in stage 5. Patients with low income were more common in stages 2 (44.2%) and 5 (47.4%), while those with medium or high income predominated in stage 1 (Table 3). These differences were statistically significant (p<0.001). Regarding educational level, there were no significant differences between stages (p=0.2), but there was a decreasing trend in the proportion of patients with higher education in advanced stages – from 22.5% in stage 2 to 11.3% in stage 4. When analyzing anthropometric parameters, the mean body weight was lowest in stage 1 (79.6±19.3 kg) and highest in stage 2 (83.8±16.6 kg), with a comparable value in stages 3 and 4 (~83 kg), followed by a further decrease in stage 5 (79.9±19.9 kg). Differences were significant (p=0.002). Mean height did not vary significantly between groups (p=0.8).

BMI followed a similar pattern: the mean value was 28.4 kg/m^2 in stage 1, increasing to 29.7 kg/m^2 in stage 2, and remaining above 29 kg/m^2 in stages 3 and 4. In stage 5, BMI was 29.1 kg/m^2, but with increased variability (Table 4). Differences between stages were statistically significant (p=0.003).

Etiologic features of CKD

The etiologic analysis of the enrolled patients revealed significant variations in the distribution of the main causes of CKD according to the stage of the disease, from 1 to 5, as described below:

- *tubulointerstitial nephropathy* had a higher prevalence in early stages of CKD. Thus, 66.8% of stage 1 patients had this etiology, followed by 58.1% in stage 2 and 61.0% in stage 3. In contrast, the proportion decreased in advanced stages: 49.0% in stage 4 and 50.0% in stage 5 (Table 2). Differences between groups were statistically significant (χ^2=17, p=0.002), suggesting a predominant involvement of this pathogenic mechanism in the early stages of CKD.
- *renal lithiasis* was significantly associated with stages 1 and 2, in which more than half of the patients reported a history of lithiasis (53.7% and 57.4%, respectively). In contrast, only 33.3% of patients had lithiasis in stage 3, and 37.1% in stage 4. In end-stage (5), lithiasis was virtually absent, with a prevalence of only 3.8% (χ^2=93, p<0.001) (Table 2). This pattern suggests that lithiasis has a limited contribution to disease progression to end-stage renal failure.
- *glomerulonephritis* was present in 39.7% of patients in stage 1 and 30.6% in stage 2, with a minimum of 28.2% in stage 3 (Table 2). The proportion increased again in advanced stages: 37.7% in stage 4 and 50.0% in stage 5 (p=0.002), indicating that glomerulonephritis may have an important impact in severe cases of kidney damage.
- hereditary or congenital diseases (in our case there were only patients with autosomal dominant polycystic autosomal dominant disease, diagnostic being placed on clinical data and family history) showed a gradual increase in frequency with advancing CKD. From 14.7% in stage 1 and 16.3% in stage 2, the proportion rose to 19.0% in stage 3, 24.5% in stage 4 and 32.1% in stage 5 (p=0.002) (Table 2), suggesting a progressive influence of these conditions in the deterioration of renal function.
- associated comorbidities:
  - *diabetes mellitus* was one of the most important comorbidities associated with CKD. It was present in 67.1% of stage 1 and 61.2% of stage 2 patients. As the disease progressed, the proportion of diabetics increased significantly: 74.4% in stage 3, 80.8% in stage 4 and 82.1% in stage 5 (p<0.001) (Table 2). This supports the hypothesis of the role of diabetes in both the initiation and progression of CKD.
  - *hypertension* was almost universal in the study group, increasing significantly with the severity of CKD. The prevalence of hypertension was 84.7% in stage 1, increasing to 93.0% in stage 2, 97.9% in stage 3, 98.7% in stage 4 and reaching 100% in stage 5 (p<0.001) (Table 2), confirming the central role of hypertension both as an etiologic factor and as an effect of renal deterioration.

Mean duration of renal disease progression ranged from 2.3 to 3.0 years, with significant differences between groups (p=0.025) (Table 5). The mean value was highest in stage 1 (2.6±1.6 years) and lowest in stages 2 (2.3±1.0 years) and 5 (2.3±1.6 years).

Table 3. Socioeconomic profile and educational level of patients correlated with the severity of CKD

Stage	1, N = 307*	95% CI**	2, N = 258*	95% CI**	3, N = 195*	95% CI**	4, N = 151	95% CI**	5, N = 78*	95% CI**	Test Statistic	p-value***
Household income											69	<0.001
Very low	85 (27.7%)	23%, 33%	81 (31.4%)	26%, 37%	61 (31.3%)	25%, 38%	50 (33.1%)	26%, 41%	22 (28.2%)	18%, 38%		
Low	68 (22.1%)	18%, 27%	114 (44.2%)	38%, 50%	74 (37.9%)	31%, 45%	50 (33.1%)	26%, 41%	37 (47.4%)	36%, 59%		
Medium	111 (36.2%)	31%, 42%	37 (14.3%)	10%, 19%	46 (23.6%)	18%, 30%	35 (23.2%)	16%, 30%	16 (20.5%)	12%, 29%		
Above average	18 (5.9%)	3.2%, 8.5%	17 (6.6%)	3.6%, 9.6%	9 (4.6%)	1.7%, 7.6%	9 (6.0%)	2.2%, 9.7%	2 (2.6%)	-0.94%, 6.1%		
High	25 (8.1%)	5.1%, 11%	9 (3.5%)	1.2%, 5.7%	5 (2.6%)	0.35%, 4.8%	7 (4.6%)	1.3%, 8.0%	1 (1.3%)	-1.2%, 3.8%		
Educational status											16	0.2
Secondary education	103 (33.6%)	28%, 39%	83 (32.2%)	26%, 38%	67 (34.4%)	28%, 41%	67 (44.4%)	36%, 52%	28 (35.9%)	25%, 47%		
High school education	29 (9.4%)	6.2%, 13%	20 (7.8%)	4.5%, 11%	20 (10.3%)	6.0%, 15%	11 (7.3%)	3.1% , 11%	11 (14.1%)	6.4%, 22%		
Medium education	111 (36.2%)	31%, 42%	97 (37.6%)	32%, 44%	69 (35.4%)	29%, 42%	56 (37.1%)	29%, 45%	23 (29.5%)	19%, 40%		
Higher education	64 (20.8%)	16%, 25%	58 (22.5%)	17%, 28%	39 (20.0%)	14%, 26%	17 (11.3%)	6.2%, 16%	16 (20.5%)	12%, 29%		

*Note: *Mean (SD); **Confidence Interval (CI); ***Kruskal-Wallis rank sum test; Pearson's Chi-squared test*

Table 4. Analysis of anthropometric indicators: body weight and BMI in the study group

Stage	1, N = 307*	95% CI**	2, N = 258*	95% CI**	3, N = 195*	95% CI**	4, N = 151*	95% CI**	5, N = 78*	95% CI**	Test Statistic	p-value***
Mass (kg)	79.6 (19.3) 76.0 (23.0) 6.0 160.0	77, 82	83.8 (16.6) 82.0 (22.0) 37.0 145.0	82, 86	83.2 (16.0) 82.0 (22.5) 50.0 130.0	81, 85	83.0 (18.1) 81.0 (23.0) 8.0 135.0	80, 86	79.9 (19.9) 75.5 (25.8) 53.0 168.0	75, 84	17	0.002
Height(cm)	167.6 (8.1) 167.0 (9.0) 150.0 205.0	167, 168	167.9 (7.8) 166.5 (9.8) 150.0 192.0	167, 169	168.3 (7.9) 168.0 (10.0) 150.0 192.0	167, 169	168.8 (8.8) 167.0 (9.5) 148.0 195.0	167, 170	168.2 (8.0) 167.5 (10.0) 150.0 186.0	166, 170	1.7	0.8
BMI	28.4 (6.9) 27.6 (7.1) 15.6 61.6	28, 29	29.7 (5.8) 28.8 (6.6) 15.2 50.8	29, 30	29.5 (5.7) 28.7 (7.4) 17.8 50.2	29, 30	29.4 (6.0) 28.4 (6.7) 16.0 56.2	28, 30	29.1 (8.6) 26.6 (7.0) 19.7 69.5	27, 31	16	0.003

*Note: *Mean (SD); **Confidence Interval (CI); *** Kruskal-Wallis rank sum test; Pearson's Chi-squared test; BMI – body mass index*

Table 5. Etiologic features of CKD

Stage/etiology	1, N = 307*	95% CI**	2, N = 258*	95% CI**	3, N = 195*	95% CI**	4, N = 151*	95% CI**	5, N = 78*	95% CI**	Statistic Test	p-value***
Tubulointerstitial nephropathy											17	0.002
Yes	205 (66.8%)	62%, 72%	150 (58.1%)	52%, 64%	119 (61.0%)	54%, 68%	74 (49.0%)	41%, 57%	39 (50.0%)	39%, 61%		
No	102 (33.2%)	28%, 38%	108 (41.9%)	36%, 48%	76 (39.0%)	32%, 46%	77 (51.0%)	43%, 59%	39 (50.0%)	39%, 61%		
Renal failure											93	<0.001
Yes	165 (53.7%)	48%, 59%	148 (57.4%)	51%, 63%	65 (33.3%)	27%, 40%	56 (37.1%)	29%, 45%	3 (3.8%)	-0.42%, 8.1%		
No	142 (46.3%)	41%, 52%	110 (42.6%)	37%, 49%	130 (66.7%)	60%, 73%	95 (62.9%)	55%, 71%	75 (96.2%)	92%, 100%		
Glomerulonephritis											17	0.002
Yes	122 (39.7%)	34%, 45%	79 (30.6%)	25%, 36%	55 (28.2%)	22%, 35%	57 (37.7%)	30%, 45%	39 (50.0%)	39%, 61%		
No	185 (60.3%)	55%, 66%	179 (69.4%)	64%, 75%	140 (71.8%)	65%, 78%	94 (62.3%)	55%, 70%	39 (50.0%)	39%, 61%		
Inherited/congenital diseases											17	0.002
Yes	45 (14.7%)	11%, 19%	42 (16.3%)	12%, 21%	37 (19.0%)	13%, 24%	37 (24.5%)	18%, 31%	25 (32.1%)	22%, 42%		
No	262 (85.3%)	81%, 89%	216 (83.7%)	79%, 88%	158 (81.0%)	76%, 87%	114 (75.5%)	69%, 82%	53 (67.9%)	58%, 78%		
Diabetes mellitus											26	<0.001
Yes	206 (67.1%)	62%, 72%	158 (61.2%)	55%, 67%	145 (74.4%)	68%, 80%	122 (80.8%)	75%, 87%	64 (82.1%)	74%, 91%		
No	101 (32.9%)	28%, 38%	100 (38.8%)	33%, 45%	50 (25.6%)	20%, 32%	29 (19.2%)	13%, 25%	14 (17.9%)	9.4%, 26%		
Hypertension											52	<0.001
Yes	260 (84.7%)	81%, 89%	240 (93.0%)	90%, 96%	191 (97.9%)	96%, 100%	149 (98.7%)	97%, 100%	78 (100.0%)	100%, 100%		
No	47 (15.3%)	11%, 19%	18 (7.0%)	3.9%, 10%	4 (2.1%)	0.06%, 4.0%	2 (1.3%)	-0.50%, 3.1%	0 (0.0%)	0.00%, 0.00%		
CKD duration (years)	2.6 (1.6) 3.0 (2.0) 1.0 15.0	2.4, 2.8	2.3 (1.0) 2.0 (2.0) 1.0 5.0	2.1, 2.4	2.5 (2.0) 2.0 (2.0) 1.0 13.0	2.2, 2.7	2.8 (2.2) 2.0 (2.0) 1.0 15.0	2.4, 3.2	2.3 (1.6) 2.0 (2.0) 1.0 10.0	2.0, 2.7	11	0.025
eGFR-CKD-EPI	94.6 (30.9) 100.0 (15.5) 2.0 184.0	91, 98	75.2 (12.6) 75.0 (17.0) 32.0 125.0	74, 77	45.5 (14.8) 44.0 (15.5) 7.0 118.0	43, 48	29.9 (23.4) 23.0 (8.0) 11.0 131.0	26, 34	9.6 (3.2) 10.0 (5.0) 2.0 17.0	8.9, 10	636	<0.001

*Note: *Mean (SD), median (IQR); **Confidence Interval (CI); *** Kruskal-Wallis rank sum test; Pearson's Chi-squared test*

eGFR (calculated by the CKD-EPI formula) decreased significantly throughout disease progression. Thus, the mean value of GFR was 94.6 ml/min/1.73m² in stage 1, 75.2 in stage 2, 45.5 in stage 3, 29.9 in stage 4 and only 9.6 ml/min/1.73m² in stage 5 (p<0.001) (Table 5), confirming the consistency of the classification of patients according to the severity of renal impairment.

Biological parameters according to CKD stage

The distribution of patients with CKD according to disease stages revealed statistically significant differences in most of the biological parameters analyzed (Table 6). The progression of CKD was associated with relevant changes in renal function and metabolic and hematologic parameters, suggesting systemic deterioration as the disease progressed.

Table 6. Biological parameters by stage of CKD

Batch	1, N = 307*	95% CI**	2, N = 258*	95% CI**	3, N = 195*	95% CI**	4, N = 151*	95% CI**	5, N = 78*	95% CI**	Statistic Test	p-value***
Hb	127.6 (18.8) 129.0 (19.5) 62.0 173.0	125, 130	130.5 (17.3) 131.0 (22.0) 62.0 193.0	128, 133	123.3 (19.7) 124.0 (26.5) 65.0 165.0	121, 126	114.1 (19.6) 113.0 (21.5) 63.0 181.0	111, 117	96.8 (16.9) 96.5 (17.8) 60.0 136.0	93, 101	196	**<0.001**
Serum creatinine	100.8 (135.0) 65.0 (18.5) 34.4 1,449.2	86, 116	85.5 (18.5) 82.9 (17.5) 55.1 198.1	83, 88	144.8 (72.8) 133.8 (52.4) 52.0 680.1	135, 155	230.1 (79.3) 230.5 (85.1) 44.6 411.1	217, 243	533.3 (253.5) 468.7 (204.2) 58.7 1,691.0	476, 590	595	**<0.001**
Serum urea	7.1 (6.8) 5.2 (2.5) 2.5 63.0	6.3, 7.8	6.7 (3.9) 6.2 (2.5) 2.6 58.0	6.3, 7.2	10.4 (4.9) 9.5 (4.2) 3.7 53.9	9.7, 11	14.9 (5.6) 13.9 (6.9) 3.7 32.6	14, 16	25.9 (10.1) 23.7 (11.1) 12.5 65.1	24, 28	496	**<0.001**
Serum albumin	42.0 (4.8) 42.8 (5.0) 24.0 50.8	41, 42	42.4 (4.2) 43.0 (4.9) 18.2 50.9	42, 43	40.5 (5.1) 41.4 (5.4) 20.8 49.2	40, 41	39.1 (5.8) 40.9 (6.4) 17.9 50.9	38, 40	39.7 (5.6) 40.4 (6.0) 18.6 50.5	38, 41	59	**<0.001**
Total protein	68.9 (7.0) 69.4 (8.2) 40.7 88.6	68, 70	69.0 (6.6) 69.7 (7.2) 33.2 85.9	68, 70	67.5 (7.4) 67.7 (8.8) 41.4 94.2	66, 69	66.9 (8.0) 67.7 (9.5) 39.0 94.2	66, 68	66.0 (8.6) 66.5 (11.5) 33.2 85.8	64, 68	21	**<0.001**
Uric acid	315.6 (111.0) 305.9 (132.6) 126.6 765.2	303, 328	349.1 (104.1) 334.8 (119.6) 115.9 859.5	336, 362	408.0 (118.3) 400.6 (152.6) 189.3 809.9	391, 425	453.5 (140.9) 442.0 (148.2) 130.1 995.5	431, 476	469.4 (102.8) 448.4 (129.0) 291.0 774.9	446, 493	210	**<0.001**
K	4.5 (0.5) 4.5 (0.5) 2.4 6.3	4.4, 4.5	4.6 (0.5) 4.6 (0.6) 3.2 6.3	4.5, 4.6	4.8 (0.6) 4.8 (0.7) 2.3 6.8	4.7, 4.9	4.9 (0.7) 4.9 (0.9) 2.7 6.7	4.8, 5.0	5.4 (0.8) 5.4 (1.1) 3.5 8.0	5.2, 5.5	124	**<0.001**
Na	142.8 (2.5) 143.0 (3.2) 130.0 149.8	143, 143	143.0 (2.8) 143.1 (3.1) 125.4 149.1	143, 143	143.0 (2.9) 143.1 (3.3) 130.3 149.4	143, 143	142.7 (2.9) 143.0 (3.6) 133.8 149.2	142, 143	142.8 (3.1) 143.0 (3.9) 133.2 149.0	142, 143	1.8	0.8
Total Ca	2.4 (0.1) 2.4 (0.2) 1.7 3.0	2.3, 2.4	2.3 (0.1) 2.4 (0.2) 1.9 2.9	2.3, 2.4	2.3 (0.2) 2.3 (0.2) 1.6 3.0	2.3, 2.3	2.3 (0.2) 2.3 (0.2) 1.7 2.8	2.3, 2.3	2.2 (0.2) 2.2 (0.3) 1.6 2.9	2.1, 2.2	69	**<0.001**
Ionic Ca	1.1 (0.1) 1.1 (0.1) 0.3 1.7	1.1, 1.1	1.1 (0.1) 1.1 (0.1) 0.9 1.7	1.1, 1.1	1.1 (0.1) 1.1 (0.1) 0.7 1.4	1.1, 1.1	1.0 (0.1) 1.1 (0.1) 0.8 1.3	1.0, 1.1	1.0 (0.1) 1.0 (0.1) 0.5 1.3	0.97, 1.0	65	**<0.001**
Microalbuminuria	147.6 (492.6) 9.7 (45.3) 0.0 4,510.2	92, 203	144.4 (704.8) 7.7 (30.4) 0.0 8,284.4	58, 231	275.7 (724.8) 22.0 (135.8) 0.0 6,620.0	173, 378	497.6 (849.7) 102.0 (560.3) 0.0 4,856.1	361, 634	549.5 (1,093.7) 136.1 (483.0) 0.0 7,401.5	303, 796	90	**<0.001**

*Note: *Mean (SD), median (IQR); **Confidence Interval (CI); ***Kruskal-Wallis rank sum test*

Hemoglobin values decreased progressively from stage 1 to stage 5, indicating the onset and worsening of anemia in correlation with declining renal function ($p<0.001$, Kruskal-Wallis test). At the same time, serum creatinine and serum urea increased significantly from early stages to stage 5, reflecting the accumulation of nitrogen catabolism products in the blood ($p<0.001$).

Albumin and total protein showed decreasing values in patients with advanced stages of CKD, suggesting the possible onset of nephrotic syndrome or protein malnutrition. Uricemia significantly increased in parallel with disease progression ($p<0.001$), as did proteinuria, which was significantly higher in stages 4 and 5 than in stages 1-2 (Table 6).

Electrolyte levels also showed significant differences: serum potassium increased progressively up to stage 5 ($p<0.001$), while sodium showed insignificant variations between stages ($p=0.8$). Total and ionic calcium levels decreased significantly in advanced stages ($p<0.001$), consistent with CKD-specific disturbances in mineral and bone metabolism.

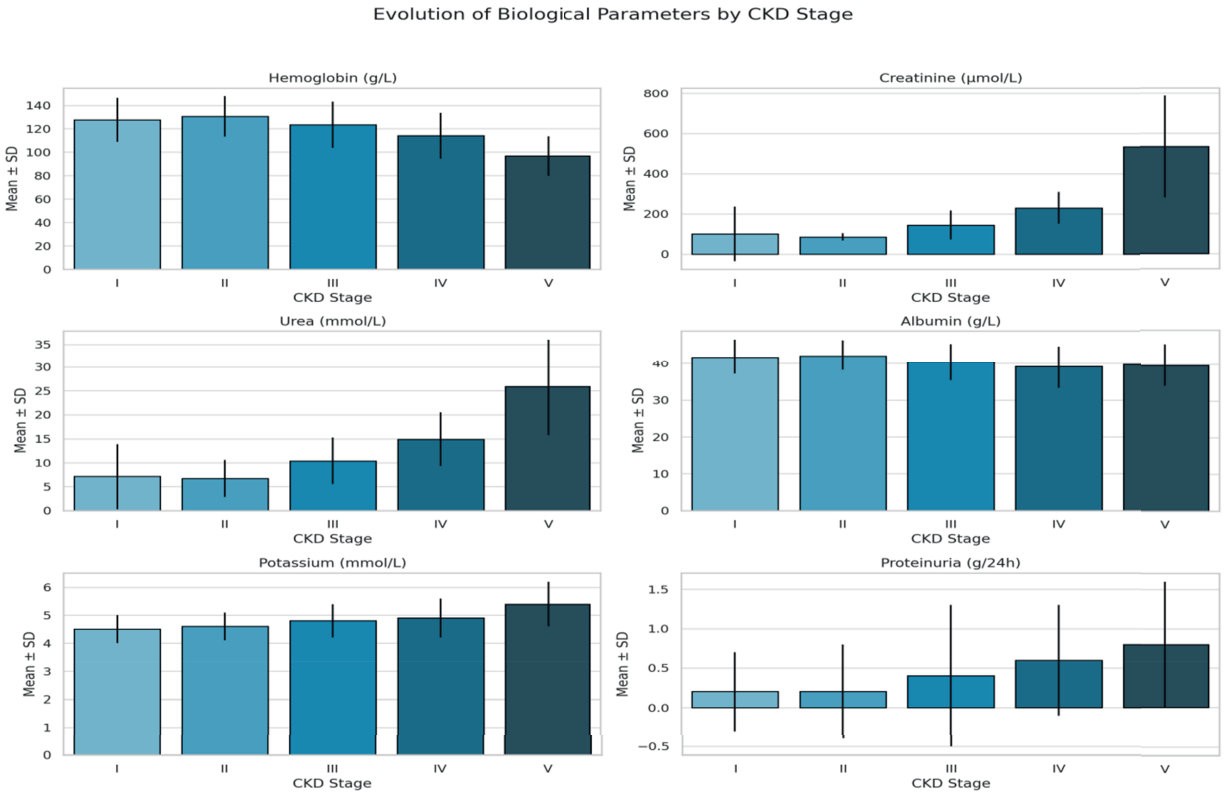


Figure 1. Evolution of biolo gical parameters by CKD stages.

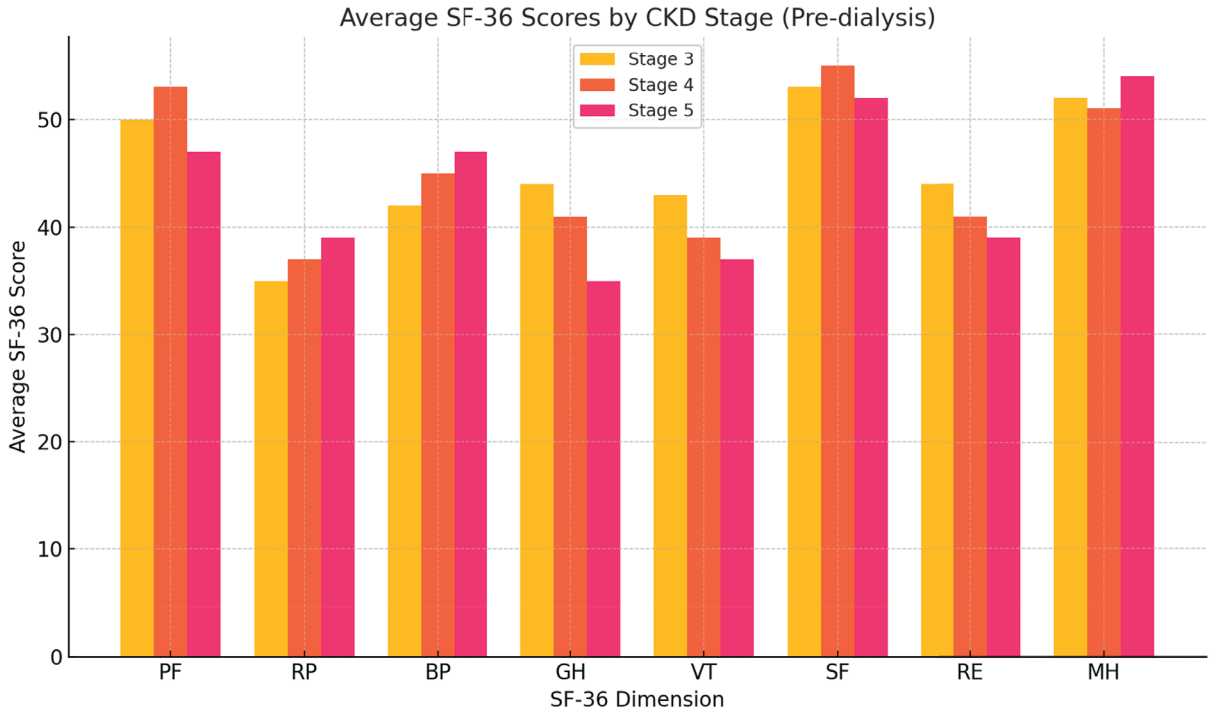


Figure 2. The mean values of the eight SF-36 dimensions in patients with CKD.
In pre-dialytic stages 3, 4 and 5 show a trend of decreasing QoL in stage 4 (represented by orange bars), followed by a slight improvement in pre-dialytic stage 5 (red bars) compared to stage 4. However, all scores remain below the levels recorded in the general population of similar age (e.g. in the healthy adult population, the mean score for Physical Functioning exceeds 80 points).

Table 7. Gender comparison of mean SF-36 domain scores (0-100; higher scores reflect a better QoL)

Domain SF-36	*Females (n=662), mean (SD)*	*Males (n=327), mean (SD)*	*p-value*
Physical function (PF)	44.5 (26.0)	55.2 (27.4)	<0.001
Physical role (physical activity limitation)	33.8 (33.8)	39.1 (36.0)	0.039
Body pain	41.4 (17.8)	47.3 (18.6)	<0.001
General health (GH)	33.3 (15.9)	35.9 (15.8)	0.002
Energy/Obust (vitality)	40.9 (14.6)	46.2 (15.7)	<0.001
Social function (SF)	51.4 (19.1)	55.7 (19.4)	0.008
Emotional state (mental well-being)	53.3 (14.9)	56.8 (14.8)	0.002
Emotional role (limiting emotional activities)	39.4 (37.8)	48.5 (39.2)	<0.001
Physical component SF-12 (PCS)	32.6 (8.1)	35.2 (8.7)	<0.001
Mental component SF-12 (MCS)	40.9 (8.2)	43.1 (8.0)	<0.001

Note: p-value<0.05

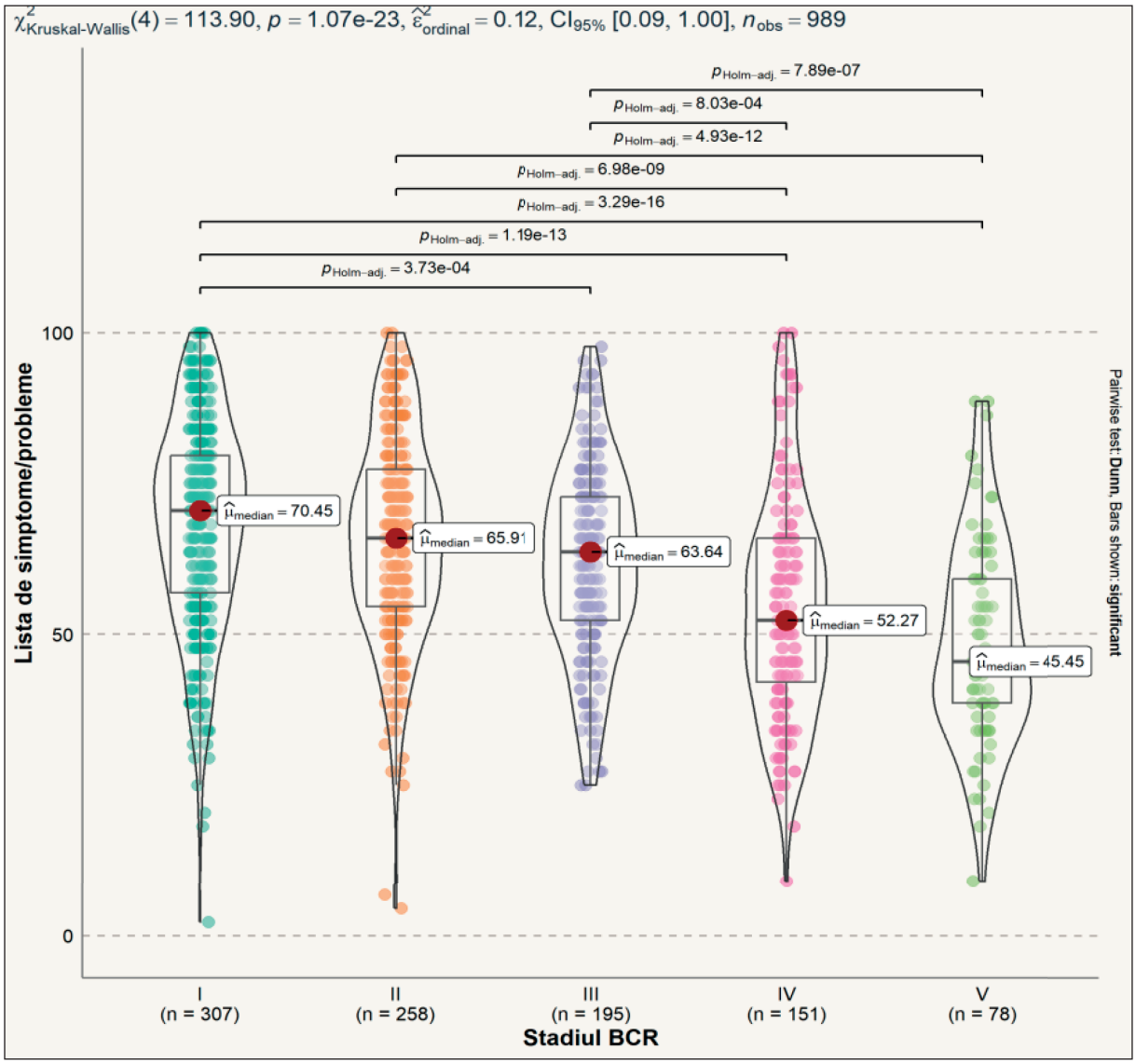


Figure 3. Evolution of scores for the domain "Symptom/problem list" (KDQOL-36) according to the progression of CKD (stages 1-5).

Microalbuminuria was significantly higher in stages 4-5 compared with early stages (p<0.001), suggesting progressive glomerular filter impairment even in the absence of massive proteinuria.

These associations were tested using the Kruskal-Wallis test for nonparametric continuous variables. The *p* values obtained were <0.001 for most parameters, indicating statistically significant

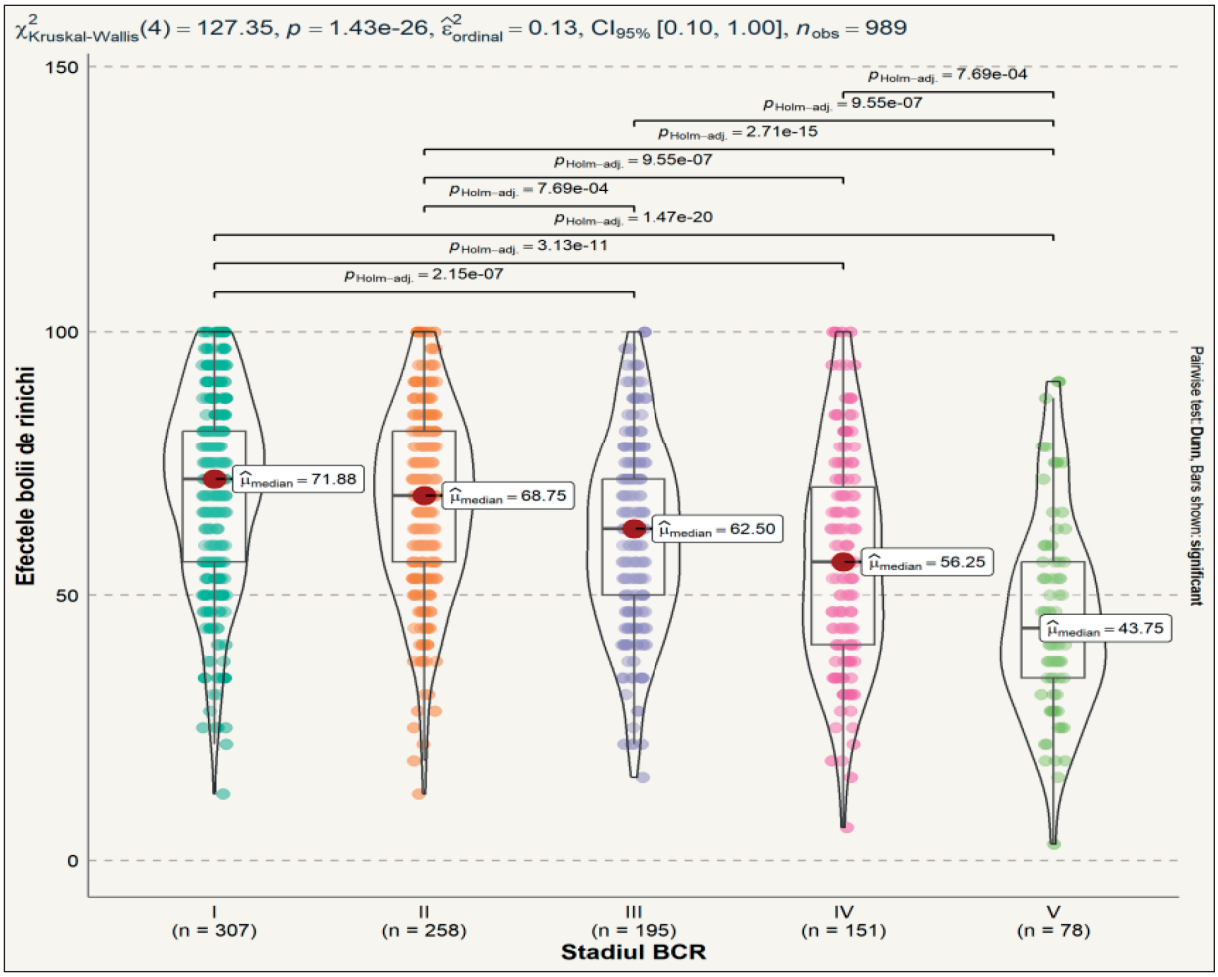


Figure 4. Change in scores for the domain "Effects of kidney disease" in relation to stages of chronic kidney disease (1-5).

differences between disease stages. Figure 1 graphically demonstrates the evolution of six main biological parameters according to the stages of CKD.

Comparative analysis of QoL by gender in patients with CKD

HRQoL was analyzed using the KDQOL-SF questionnaire, which includes both the general components of the SF-36 (eight subscales) and aspects specific to CKD. The results showed significant gender differences in most dimensions of QoL, with women reporting lower scores than men, suggesting a lower QoL. Table 7 presents the mean values and standard deviations for each SF-36 domain, differentiated by gender, together with the statistical significance of these differences.

All general domains of QoL are lower in women compared to men, with significant differences for each sub-score of the SF-36. The largest gaps, of about 5-10 points, are found in physical functioning, bodily pain, vitality and emotional role, with women reporting more severe physical and emotional limitations, more intense pain and more fatigue than men. Also, the summary scores of the physical and mental components (PCS and MCS of the SF-12) are significantly lower in women (differences of approximately 2.5-2.6 points for PCS and 2.2 points for MCS, $p<0.001$), indicating a more negative perception of health status among women.

QoL analysis in patients with CKD in pre-dialysis stages

Assessment of QoL in patients with CKD in the pre-dialytic stages demonstrated that stage 4 individuals have the lowest scores in most of the domains analyzed, showing a progressive deterioration of QoL with disease progression. However, paradoxically, pre-dialytic stage 6 patients reported slightly higher scores compared to stage 4 patients on all measured dimensions, although the values remain significantly below the general population (Figure 2). This apparent discrepancy may be explained by factors such as patient selection (e.g. stage 5 patients without dialysis generally being younger or having a better coping capacity), survival bias (patients with severely impaired QoL in stage 5 likely already having undergone dialysis or having died), and psychological coping mechanisms

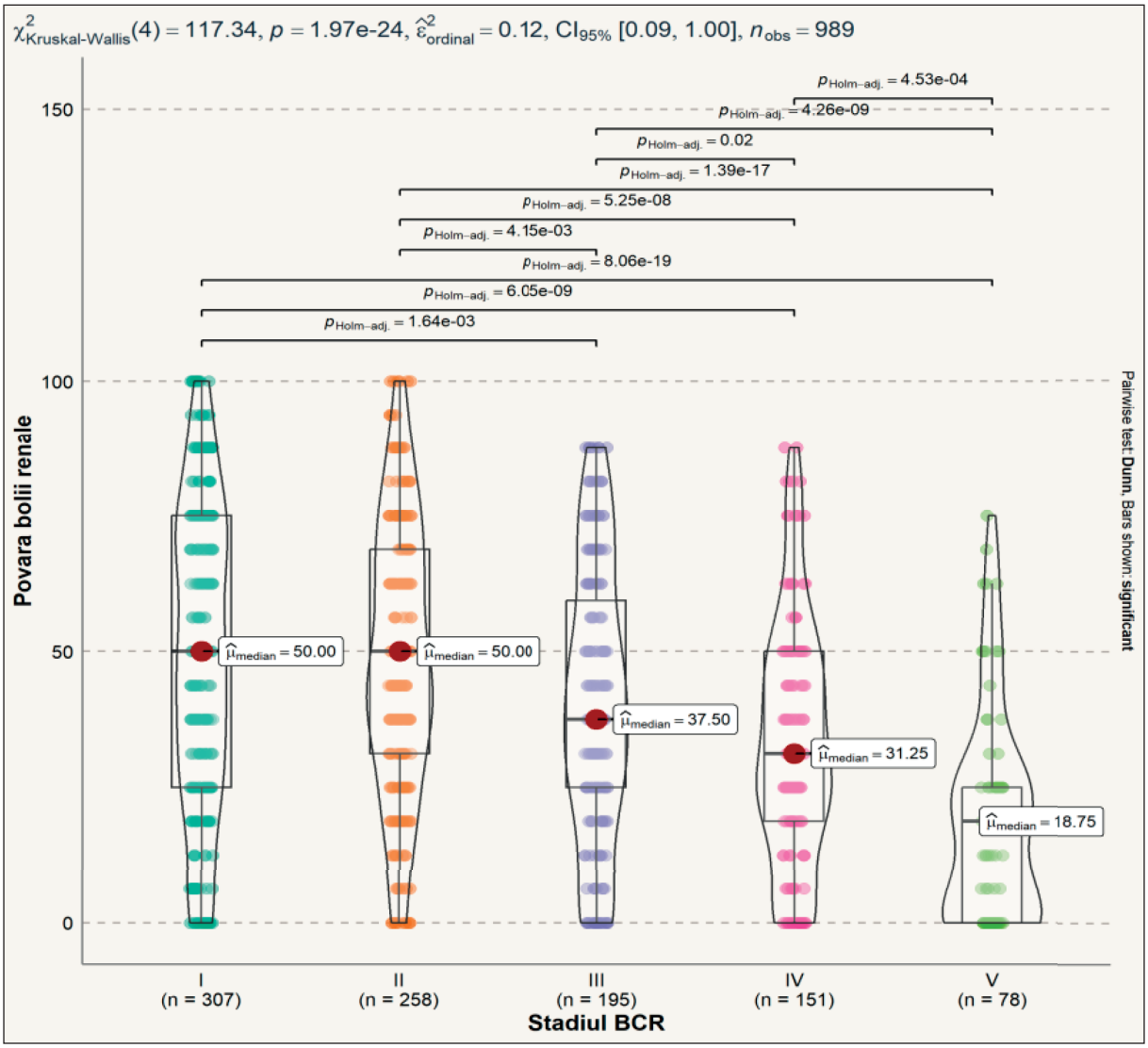


Figure 5. Progressive dynamics of perceived burden of kidney disease at different stages of CKD.

and re-evaluation of perceived QoL, which may cause advanced stage patients to report a slightly better subjective status than would be expected.

Results of kidney disease specific domains in the KDQOL

The kidney-specific KDQOL-36 KDQOL-36 questionnaire scores include domains such as "Symptom/Problem List", "Effects of Kidney Disease", "Burden of Illness" and "Work Status" and are validated tools for assessing QoL in patients with CKD or on dialysis. In the analyzed group, the domain 'Symptom/problem list' – which measures the frequency and severity of physical manifestations associated with CKD (e.g. muscle cramps, bone pain, dyspnea, pruritus, loss of appetite, etc.) – showed a significant reduction in scores with disease progression. On a scale from 0 to 100 (where 100 indicates complete absence of symptoms), the mean score was about 68 in stage 1, decreasing to about 62 in stage 3 and reaching a minimum of 48.6 in stage 5 (statistically significant differences, $p<0.001$) (Figure 3). These data suggest that patients in stage 5 experience about half of the listed symptoms, whereas in stage 1 only about 30% of symptoms are reported to be present.

The score for "Effects of kidney disease on daily life" in the KDQOL-36 reflects the impact that CKD has on patients' daily activities, including social life, diet and personal plans. This indicator followed a downward trend as the disease progressed: from a mean score of about 65.6 in stage 2, to 63.6 in stage 1, down to about 48.4 in stage 5 (estimated based on a median of 52.3 for this stage) (Figure 4). However, compared to the evolution of the symptom score, the decline of this indicator is less steep, which may suggest a capacity to adapt and maintain a certain degree of functionality in some patients.

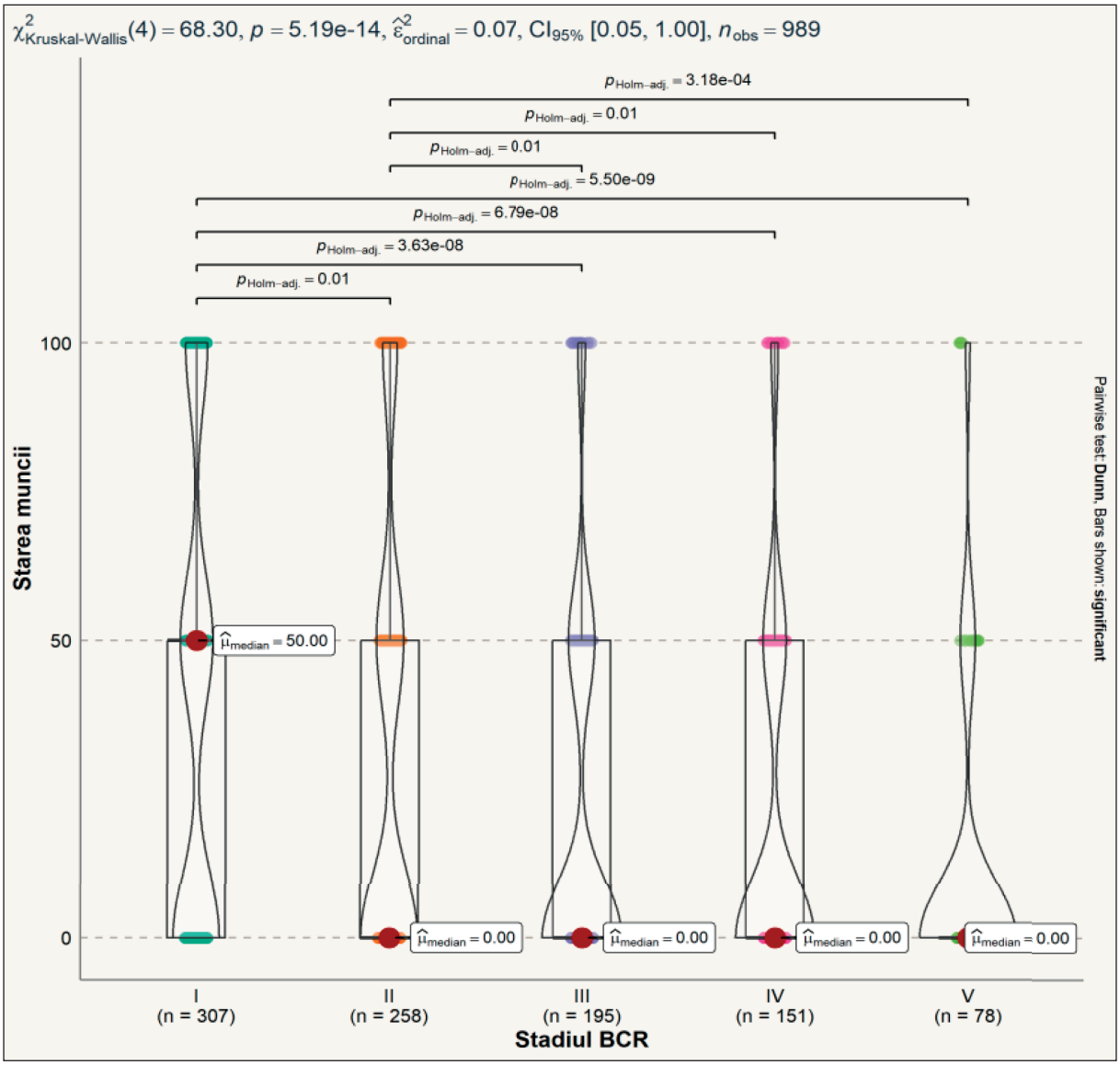


Figure 6. Changes in self-assessed work capacity according to disease stage.

The "Burden of kidney disease" domain proves to be one of the domains most affected by the progression of CKD, as it captures how patients perceive the difficulties associated with managing the condition – including feelings of dependency, impact on family or psychological distress. According to the data analyzed, the mean score for this indicator decreases significantly from about 70.5 in stage 2 to only 45.5 in stage 5 (Figure 5). This difference suggests that in the advanced stages, patients experience a much more intense sense of constraint and discomfort related to the disease, whereas in the early stages the burden is perceived as considerably less and more manageable.

The domain "Work status" refers to patients' ability to perform productive activities, either at work or in the household, and is strongly influenced by the stage of CKD, but also by age. In the study sample, patients in stages 1-2 had relatively high scores, reflecting active participation in either work or household activities, whereas in stage 5, where most patients were retired or unable to work due to their clinical condition, scores were significantly lower (Figure 6).

Discussion

The present study provides a comprehensive perspective on HRQoL in patients with CKD in the Republic of Moldova, stages 1-5, not yet receiving hemodialysis treatment, using the KDQoL-36 questionnaire. The results show a significant deterioration of HRQoL with disease progression, confirming the role of CKD stage as a key predictor of QoL[16]. Consistent with the literature, patients of older age had significantly lower scores in physical and mental domains, as well as an increased perception of disease burden, with

these trends evident in physical component summary (PCS) and KSS scores. Retirement, often associated with advanced age and decreased physical functionality, also correlated with reduced HRQoL scores[17]. These observations underscore the need for personalized strategies that integrate HRQoL assessment into routine clinical practice and address psychosocial factors that influence patient perception of illness[18].

In contrast to some previous studies that have not identified significant variations in HRQoL in the early stages of CKD[19], our results highlight a progressive decline in the physical components of HRQoL with disease progression[20]. Especially in stages 3-5, the patients reported a considerable reduction in physical functioning and energy levels[21]. These findings are consistent with other research that has shown deterioration of physical function and decreased vitality in patients with advanced CKD, suggesting that impaired somatic status and marked fatigue are major aspects that negatively influence the perception of QoL in this population[22].

Biologically, progression to stages 4-5 has been associated with elevated creatinine and urea values and significant decreases in hemoglobin and albumin, reflecting progressive renal dysfunction and systemic metabolic disturbances[23]. Anemia, commonly seen in advanced stages, is a consequence of erythropoietin deficiency and chronic inflammation and is associated with reduced QoL[24]. Also, hyperkalemia and hypocalcemia observed in advanced stages confirm worsening electrolyte imbalances and mineral-bone disorder[25].

The statistically significant association between CKD stages and sociodemographic variables – such as age, gender, occupation and income – corroborates with the literature which argues that ageing, poor socioeconomic status and reduced access to care contribute to worsening CKD[26]. Comorbidities such as diabetes mellitus and hypertension were more prevalent in advanced stages, reinforcing evidence that recognizes them as major modifiable risk factors for disease progression[27].

In terms of HRQoL, the analysis revealed significant gender differences, with women scoring lower on all 8 SF-36 subscales and on kidney disease-specific dimensions[28]. These differences may be explained by biological and psychosocial factors, such as women's higher tendency to report depressive symptoms, heightened perception of functional limitations and multiple family roles[29].

It is noteworthy that KDQoL-36 scores reflected a marked impact in the domains "Effects of kidney disease" and "Burden of kidney disease", suggesting a profound psychosocial influence on patients in advanced stages, like data in the international literature[30]. Interestingly, a slight paradoxical improvement in HRQoL scores was observed in pre-dialysis stage 5, a phenomenon possibly attributed to selection of better adapted patients or psychological coping mechanisms[31].

The negative correlation between disease severity and self-rated work capacity emphasizes the profound socio-professional impact of HRQoL, confirming the results of other studies on loss of independence and decreased productivity[32].

Limitations of the study: cross-sectional design, which limits the interpretation of causality, and the potential influence of confounding variables such as social support and unquantified comorbidities. However, the use of a validated instrument such as the KDQoL-36 and the coverage of all stages of CKD provides significant value to the results. Future longitudinal studies with larger sample sizes and including patients on RRT are needed to fully assess HRQoL dynamics across the entire evolution of CKD.

Systematic integration of HRQoL assessments into clinical practice, together with a multidisciplinary approach – including symptom control, educational interventions and psychosocial support – can significantly contribute to improving the QoL and functionality of patients with CKD.

Conclusions

The results of this study highlight a robust association between the severity of CKD and several clinical, biochemical and socio-demographic factors. Progression to advanced stages of CKD was correlated with significant metabolic alterations, illustrated by increases in creatinine, urea and potassium, concomitant with decreases in hemoglobin and albumin, indicating deterioration of renal function and the development of systemic complications. In addition, advanced age, the presence of major comorbidities (diabetes mellitus and hypertension), low socioeconomic status and disadvantaged occupational status were found to be important determinants of disease progression. The assessment of QoL using the KDQOL-SF instrument revealed a progressive deterioration in the physical and psychosocial dimensions of HRQoL, consistent with the progression of CKD. Significant gender differences were also observed, with a more severe impact on women, suggesting increased vulnerability among women. In view of these findings, it is necessary to develop integrated interventions that go beyond the strictly medical dimension, including psychosocial support, constant monitoring of QoL and policies to reduce inequalities in access to care. Future prevention and management strategies for CKD should be patient-centered, facilitate early identification of disease and promote

rigorous control of comorbidities, particularly among vulnerable population groups. Systematic implementation of HRQoL assessments in routine clinical practice can significantly contribute to optimizing therapeutic outcomes and increasing the quality of services provided to patients with CKD.

Author contributions

C.G., L.G., L.R., and O.A. conceived and designed the study. C.G., E.C., R.B. and A.C. performed data analysis and interpretation. E.R. and V.C. drafted the manuscript. All authors critically revised the manuscript for intellectual content, approved the final version, and agreed to be accountable for all aspects of the work.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008 (5), as well as the national law. Informed consent was obtained from the patients included in the study."

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References

1. Deng L, Guo S, Liu Y, et al. Global, regional, and national burden of chronic kidney disease and its underlying etiologies from 1990 to 2021: a systematic analysis for the Global Burden of Disease Study. *BMC Public Health*. 2025;25(1):636. doi: 10.1186/s12889-025-21851-z.
2. Jian Y, Zhu D, Zhou D, et al. ARIMA model for predicting chronic kidney disease and estimating its economic burden in China. *BMC Public Health*. 2022;22(1):2183. doi: 10.1186/s12889-022-14959-z.
3. Sosnowski R, Kulpa M, Ziętalewicz U, et al. Basic issues concerning health-related quality of life. *Cent European J Urol*. 2017;70(2):206-211. doi: 10.5173/ceju.2017.923.
4. Bonomi AE, Patrick DL, Bushnell DM, Martin M. Validation of the United States' version of the World Health Organization Quality of Life (WHOQOL) instrument. *J Clin Epidemiol*. 2000;53(1):1-12. doi: 10.1016/s0895-4356(99)00123-7.
5. Moons P, Jaarsma T, Norekvål TM. Requirements for quality-of-life reports. *Eur J Cardiovasc Nurs*. 2010;9(3):141-143. doi: 10.1016/j.ejcnurse.2010.06.002.
6. Kalantar-Zadeh K, Unruh M. Health related quality of life in patients with chronic kidney disease. *Int Urol Nephrol*. 2005;37(2):367-378. doi: 10.1007/s11255-004-0012-4.
7. Cruz MC, Andrade C, Urrutia M, et al. Quality of life in patients with chronic kidney disease. *Clinics (Sao Paulo)*. 2011;66(6):991-995. doi: 10.1590/s1807-59322011000600012.
8. Pagels AA, Söderkvist BK, Medin C, et al. Health-related quality of life in different stages of chronic kidney disease and at initiation of dialysis treatment. *Health Qual Life Outcomes*. 2012;10:71. doi: 10.1186/1477-7525-10-71.
9. Mujais SK, Story K, Brouillette J, et al. Health-related quality of life in CKD Patients: correlates and evolution over time. *Clin J Am Soc Nephrol*. 2009;4(8):1293-1301. doi: 10.2215/CJN.00180109.
10. Kalender B, Ozdemir AC, Dervisoglu E, Ozdemir O. Quality of life in chronic kidney disease: effects of treatment modality, depression, malnutrition and inflammation. *Int J Clin Pract*. 2007;61(4):569-576. doi: 10.1111/j.1742-1241.2006.01251.x.
11. Kefale B, Alebachew M, Tadesse Y, Engidawork E. Quality of life and its predictors among patients with chronic kidney disease: A hospital-based cross sectional study. *PLoS One*. 2019;14(2):e0212184. doi: 10.1371/journal.pone.0212184.
12. Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C–based equations to estimate GFR without race. *N Engl J Med*. 2021;385(19):1737-1749. doi: 10.1056/NEJMoa2102953.
13. Groppa L, Popa S, Rotaru L, et al, editors. Rheumatology and Nephrology: (book). 2nd ed. Nicolae Testemitanu State University of Medicine and Pharmacy. Chișinău: Medicina; 2018. 464 p. ISBN 978-9975-82-084
14. Societatea Romana de Nefrologie. *Kidney Disease and Quality of Life™ Short Form (KDQOL-SF™ 1.3): Versiunea în limba romana 1.3*. Bucuresti: SRN; 1995. ISBN 973-0-00214-4.
15. Peipert JD, Nair D, Klicko K, et al. Kidney Disease Quality of Life 36-Item Short Form Survey (KDQOL-36) Normative Values for the United States Dialysis Population and New Single Summary Score. *J Am Soc Nephrol*. 2019;30(4):654-663. doi: 10.1681/ASN.2018100991.
16. Kim DW, Song SH. Sarcopenia in chronic kidney disease: from bench to bedside. *Korean J Intern Med*. 2023;38(3):303-321. doi: 10.3904/kjim.2022.375.
17. Perlman RL, Finkelstein FO, Liu L, et al. Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study. *Am J Kidney Dis*. 2005;45(4):658-666. doi: 10.1053/j.ajkd.2004.12.021.
18. Fukuhara S, Lopes AA, Bragg-Gresham JL, et al. Health-related quality of life among dialysis patients on three continents: The Dialysis Outcomes and Practice Patterns Study. *Kidney Int*. 2003;64(5):1903-1910. doi: 10.1046/j.1523-1755.2003.00289.x.
19. Levey AS, Andreoli SP, DuBose T, et al. CKD: common, harmful, and treatable—World Kidney Day 2007. *Am J Kidney Dis*. 2007;49(2):175-179. doi: 10.1053/j.ajkd.2006.12.013.
20. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. *PLoS One*. 2014;9(1):e84943. doi: 10.1371/journal.pone.0084943.
21. Kovesdy CP. Management of hyperkalaemia in chronic kidney disease. *Nat Rev Nephrol*. 2014;10(11):653-662. doi: 10.1038/nrneph.2014.168.
22. Pavlović D, Katičić D, Gulin T, et al. Chronic kidney disease mineral bone disorder. *Period Biol*. 2015;117(1):81-85.
23. O'Hare AM, Choi AI, Bertenthal D, et al. Age affects outcomes in chronic kidney disease. *J Am Soc Nephrol*. 2007;18(10):2758-2765. doi: 10.1681/ASN.2007040422.
24. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl*. 2013;3(1):1-150.

25. Stevens PE, Ahmed SB, Carrero JJ, et al. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314. doi: 10.1016/j.kint.2023.10.018.
26. Hedayati SS, Yalamanchili V, Finkelstein FO. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. *Kidney Int*. 2012;81(3):247-255. doi: 10.1038/ki.2011.358.
27. Zazzeroni L, Pasquinelli G, Nanni E, et al. Comparison of Quality of Life in Patients Undergoing Hemodialysis and Peritoneal Dialysis: a Systematic Review and Meta-Analysis. *Kidney Blood Press Res*. 2017;42(4):717-727. doi: 10.1159/000484115.
28. Mapes DL, Lopes AA, Satayathum S, et al. Health-related quality of life as a predictor of mortality and hospitalization: The Dialysis Outcomes and Practice Patterns Study (DOPPS). *Kidney Int*. 2003;64(1):339-349. doi: 10.1046/j.1523-1755.2003.00072.x.
29. Finkelstein FO, Wuerth D, Finkelstein SH. Health related quality of life and the CKD patient: Challenges for the nephrology community. *Kidney Int*. 2009;76(9):946-952. doi: 10.1038/ki.2009.307.
30. Ware JE, Kosinski M, Keller SD. *SF-36 Physical and Mental Health Summary Scales: A User's Manual*. Boston, MA: The Health Institute, New England Medical Center; 1994.
31. Saran R, Robinson B, Abbott KC, et al. US Renal Data System 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States. *Am J Kidney Dis*. 2020;75(1 Suppl 1):S1-S64. doi: 10.1053/j.ajkd.2019.09.001.
32. Murray R, Zimmerman T, Agarwal A, et al. Kidney-Related Research in the United States: A Position Statement from the National Kidney Foundation and the American Society of Nephrology. *Am J Kidney Dis*. 2021;78(2):161-167. doi: 10.1053/j.ajkd.2021.04.006.