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Quantifying Fatigue in Chronic Kidney Disease: Its Correlation with Disease Severity and Biochemical Parameters

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Abstract

Background: Chronic Kidney Disease is a chronic health condition with physical and psychological impacts. This study determined the level of fatigue in patients with CKD and its association with the severity of the disease and some clinical parameters. **Methods:** A cross-sectional study was designed and performed on 80 patients with CKD who were attending the nephrology clinics and dialysis units. Structured questionnaires and a review of medical records were used to gather demographic and clinical information. Fatigue Severity Scale (FSS) was used for assessing fatigue. The clinical parameters such as estimated glomerular filtration rate (eGFR), serum creatinine, haemoglobin level, and duration of CKD were noted. The descriptive and inferential statistics were applied via SPSS version 26.0. **Results:** Participants had moderate to high fatigue reflected in a mean fatigue severity score of 42.8 ± 10.5. 47.5% of patients reported moderate fatigue and 35.0% severe fatigue. There was a significant increase in fatigue severity from the CKD 2 stage (31.4 ± 7.2) to the CKD 5 stage (53.3 ± 7.6) ($p < 0.001$). Significant positive correlations were observed between fatigue and age ($r = 0.31$, $p = 0.005$), disease duration ($r = 0.38$, $p < 0.001$), and serum creatinine levels ($r = 0.59$, $p < 0.001$). Significant negative correlations were found between fatigue and haemoglobin ($r = −0.54$, $p < 0.001$) as well as eGFR ($r = −0.62$, $p < 0.001$). Reduced eGFR ($\beta = −0.41$, $p < 0.001$), low haemoglobin ($\beta = −0.33$, $p = 0.002$) and high serum creatinine ($\beta = 0.29$, $p = 0.006$) were significant factors associated with fatigue severity in multiple regression analysis. **Conclusions:** Fatigue is a very common symptom in patients with chronic kidney disease, and gets worse as the disease advances. Fatigue severity was linked to decreased kidney function and anemia.

Keywords: Chronic Kidney Disease, Fatigue, Disease Severity, eGFR, Haemoglobin, Serum Creatinine, Nephrology, Cross-Sectional Study

Introduction

Chronic kidney disease (CKD) is a significant public health challenge that impacts millions of people around the world, and is a major cause of morbidity, mortality and health care costs [1]. Population ageing and the growing prevalence of diabetes mellitus, hypertension, and other chronic diseases are contributing to the growing burden of CKD worldwide [2]. It is a progressive and irreversible loss of kidney function that causes metabolic abnormalities, cardiovascular complications, and lowers quality of life [3,4]. In the later stages of CKD, people may have many physical and psychological problems that make it hard to carry out daily activities and maintain health [5]. Fatigue is one of the most common and troublesome symptoms reported by people with chronic kidney disease [6]. It occurs at any point in CKD and is commonly reported as one of the symptoms most significantly interfering with patients' ability to function in their daily lives[7]. Fatigue is a self-reported sensation of exhaustion, loss of energy and diminished ability to undertake physical and mental tasks, which is not improved by sleep [8].

Fatigue is not like regular tiredness and can be a constant problem in CKD that can significantly affect physical, social and emotional function [9]. The symptom can be caused by many factors as anemia, infection, metabolic disturbance, uremia, sleep disturbance, nutritional deficiency, and the burden of chronic treatment [10]. Fatigue is a multi-faceted phenomenon and is difficult to assess, so it is important to determine clinical contributors in patients who do suffer with fatigue [11]. Fatigue may impact work, social life, treatment compliance and quality of life and represents a clinically relevant topic in the care of patients with chronic kidney disease [12].

Previous studies have shown that fatigue increases with worsening kidney function and has been linked to markers of severity of kidney disease, including decreased eGFR, elevated serum creatinine, and anemia [13]. Yet, the extent and the factors that influence fatigue can differ across patient groups, so further research is needed across a variety of clinical settings. The sooner that factors contributing to fatigue are identified, potentially the sooner intervention can be made and patient-centered outcomes can be optimized. While fatigue is common among people with CKD, it is not well recognized or treated in typical clinical practice. It is important to understand the relationship between fatigue and disease severity to develop comprehensive management strategies and quality of life in affected patients [14]. In addition, assessing fatigue as a symptom based on severity of the disease may guide decision making for interventions to prevent the worsening of functional status and patient reported outcomes in a timely manner for certain individuals who are at risk.

So, the present study was undertaken to evaluate the severity of fatigue in chronic kidney disease and its association with the severity of the disease and some clinical parameters like disease duration, hemoglobin level, and kidney function.

Methodology

This is a cross-sectional study, which examined fatigue in chronic kidney disease (CKD) patients as well as its relationship with disease severity. The study (January 2022 to May 2022) was conducted in nephrology outpatient clinics and dialysis center of a tertiary care hospital. Chronic kidney disease patients (n = 80) were included in the study. The convenience sampling method was used in the recruitment of participants during the study period. The study included CKD stages 2-5 attending the nephrology clinic or dialysis unit.

Acute kidney injury, severe psychiatric disorders, active malignancy, severe infections and/or cognitive impairment that may affect the ability to complete the questionnaire were excluded. A structured questionnaire and review of medical records were used to collect data. Demographic data consisted of age, sex, duration of CKD and dialysis status. Clinical data included were CKD stage, eGFR, serum creatinine, haemoglobin concentration, and hypertension and diabetes status. The Fatigue Severity Scale (FSS) was used to assess fatigue, which is a valid scale consisting of 9 items each rated on a 7-point Likert scale. Total scores vary from 9-63, with higher scores reflecting more severe fatigue.

Patients were approached during routine clinic visits or at dialysis during the course of the clinic or dialysis. Upon informed consent, the participants answered the questionnaire and the research team retrieved relevant clinical data from the medical records. Participant characteristics and fatigue scores were summarized using descriptive statistics (frequencies, percentages, means, and standard deviations). ANOVA) was conducted to assess the differences in fatigue scores between the groups for CKD stages. Pearson correlation was used to evaluate the relationship between fatigue severity and clinical variables. Multiple linear regression was used to determine independent predictors of fatigue severity ($p < 0.05$, SPSS version 26.0). The study was approved by the departmental Head prior to the study after an informed consent. Participants' confidentiality and anonymity was protected during the course of the study.

Results

A total of 80 patients diagnosed with chronic kidney disease participated in the study. The findings describe demographic and clinical characteristics, fatigue severity, disease severity indicators, and factors associated with fatigue among CKD patients. Correlation and regression analyses were performed to determine the relationship between fatigue and disease severity. Most participants were male and aged between 40 and 59 years. Stage 3 and Stage 4 CKD were the most common disease stages, and nearly three-quarters had hypertension (Table 1).

Table 1: Demographic and Clinical Characteristics of Participants (n = 80)

Variable	Category	n (%)
Gender	Male	46 (57.5)
	Female	34 (42.5)
Age (years)	<40	14 (17.5)
	40–59	36 (45.0)
	≥60	30 (37.5)
CKD Stage	Stage 2	12 (15.0)
	Stage 3	26 (32.5)
	Stage 4	24 (30.0)
	Stage 5	18 (22.5)
Dialysis Status	Yes	32 (40.0)
	No	48 (60.0)
Hypertension	Yes	58 (72.5)
Diabetes Mellitus	Yes	35 (43.8)

Mean Fatigue Severity Score was 42.8 ± 10.5, representing that fatigue was of moderate to high level in CKD patients (Table 2). Moderate fatigue was reported by almost half of the participants, and 35.0% of participants experienced severe fatigue. There was a progressive increase in fatigue score with each stage of CKD with the highest score in Stage 5 CKD, indicating that fatigue level was significantly associated with the severity of the disease, as represented in Figure 1.

Table 2: Clinical Characteristics, Fatigue Severity, and Disease Severity Indicators (n = 80)

Variable	Category/Measure	Value
Fatigue Severity Scale Score	Mean ± SD	42.8 ± 10.5
Haemoglobin (g/dL)	Mean ± SD	9.8 ± 1.7
eGFR (mL/min/1.73m²)	Mean ± SD	28.4 ± 14.2
Serum Creatinine (mg/dL)	Mean ± SD	4.9 ± 2.3

CKD Duration (years)	Mean ± SD	5.6 ± 3.1
Fatigue Category	Mild	14 (17.5%)
	Moderate	38 (47.5%)
	Severe	28 (35.0%)
CKD Stage 2	Mean Fatigue Score ± SD	31.4 ± 7.2
CKD Stage 3	Mean Fatigue Score ± SD	38.6 ± 8.5
CKD Stage 4	Mean Fatigue Score ± SD	45.1 ± 8.7
CKD Stage 5	Mean Fatigue Score ± SD	53.3 ± 7.6
ANOVA Result	F-value	16.92
	p-value	<0.001

Mean fatigue severity increases progressively with advancing CKD stage. The difference in fatigue scores across stages is statistically significant as shown in figure 1.

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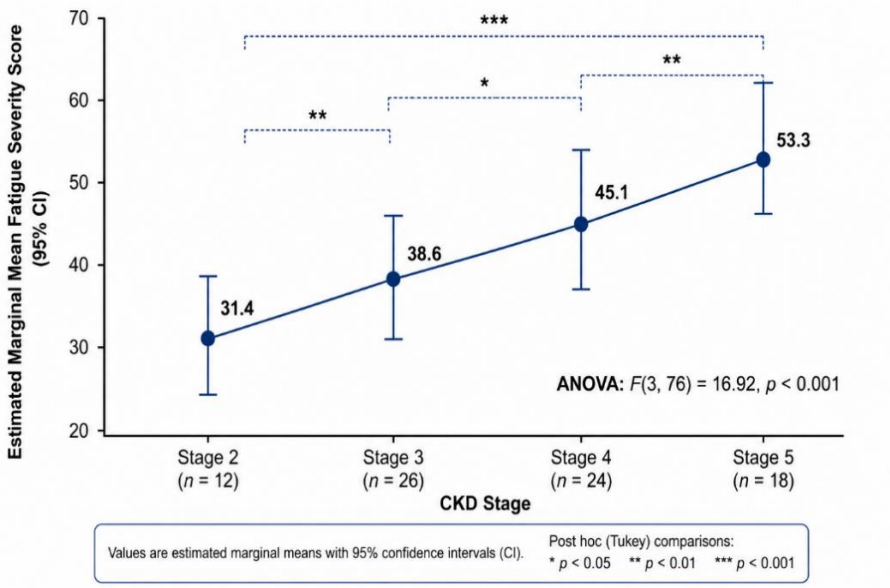
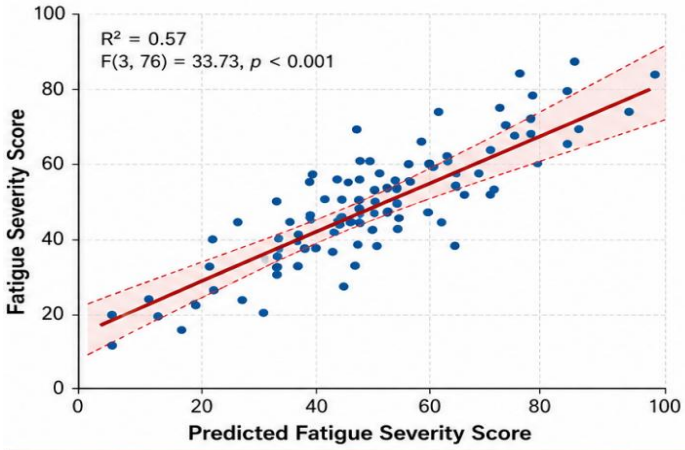


Figure 1: Mean fatigue severity scores across CKD stages (ANOVA)

Multiple regression showed that decreased eGFR (β = -0.41, p<0.001), decreased hemoglobin (β = -0.33, p = 0.002) and increased serum creatinine (β = 0.29, p = 0.006) were significant factors that correlated with fatigue severity. A global model was statistically significant (R^2 = 0.57, p < 0.001), as shown in Figure 2.



Predictor	Standardized β	p-value
eGFR (mL/min/1.73m²)	-0.41	<0.001
Hemoglobin (g/dL)	-0.33	0.002
Serum Creatinine (mg/dL)	0.29	0.006

Figure 2: Multiple Regression Analysis

Positive correlation was found between fatigue severity and age, disease duration and serum creatinine level, while hemoglobin and eGFR level were negatively correlated. In multiple regression analysis, decreased eGFR was the most significant independent predictor of fatigue severity, with decreased hemoglobin and increased serum creatinine being the next most significant. A model of regression accounted for 57% of the variability in fatigue scores and was statistically significant.

Discussion

This study was designed to assess the burden of fatigue in patients with CKD and its relationship with the severity of the disease, and certain of the clinical parameters. The key findings illustrate that fatigue symptoms are prevalent in patients with CKD. These results have significant clinical relevance. They highlight the importance of fatigue as a symptom and conclude that it must be routinely and systematically evaluated during nephrology care, rather than accepted as a common 'expected' symptom that is overlooked [14]. The associations with modifiable factors (anemia) showed that optimizing haemoglobin levels through erythropoiesis-stimulating agents or iron supplementation may alleviate fatigue [15]. The strong link between eGFR and fatigue suggests that kidney-protective medications, such as ACE inhibitors and SGLT2 inhibitors, may lessen fatigue [16].

The results of this study are consistent with previous literature. The progressive increase fatigue from stage 2 (31.4 ± 7.2) to stage 5 (53.3 ± 7.6) CKD is in line with research which reported increased prevalence of fatigue with a decline in eGFR below 30 mL/min/1.73m² [17]. Additionally, results from large population of over 400 patients with CKD demonstrated that a decrease in 10 mL/min/1.73m² eGFR resulted in 0.5-point increase in fatigue scores [18,19]. This consistency, across population and healthcare setting enhances generalizability of findings. The negative correlation between haemoglobin and fatigue was very similar to a study which identified anemia as one of the most robust and biological correlates of fatigue in CKD, mediated by reduced tissue oxygen delivery and compensatory cardiovascular strain [20,21]. Moreover, in this cohort haemoglobin was an independent predictor despite adjusting for eGFR, which corroborates the results obtained on hemodialysis patients, who stated that haemoglobin had an effect in addition to the kidney function [22]. So, anemia remains a key intervention for fatigue reduction at all CKD stages.

There is a positive correlation between serum Creatinine and fatigue, which is consistent with previous study [23]. The sample's higher percentage of severely affected patients, 40% on dialysis and the remaining patients in CKD stages 2–5, may be the cause of the substantial correlation. A positive correlation between duration of disease and fatigue is directly consistent with the previous reports which found that the uremic toxins exacerbate symptom burden [24]. The findings provide further evidence of cumulative toxic effect of chronic uremia on the energy levels of patients. This study found a positive correlation between age and fatigue aligns with previous reports. It suggests that fatigue related to aging may be explained entirely by age-related decreases in eGFR and haemoglobin [25]. There have been a few previous studies that reported the presence of the independent predictor of age in models [26]. The model demonstrated good performance with a coefficient of determination of $R2 = 0.57$, which is higher than values reported in previous studies ($R2 = 0.48$ and $R2 = 0.51$) [27]. This slight increase may be due to the inclusion of multiple clinical parameters in this model. However, 43% of variance remains unexplained, meaning other factors such as depression, sleep disorders, inflammation etc. are likely contribute significantly.

There are a number of limitations of this study. Causal inference is not possible due to the cross-sectional design. Generalizability may be limited by convenience sampling and a small sample size (n = 80). Physical and mental weariness are not distinguished by the FSS. Significant confounders were not evaluated, including depression, sleep quality, inflammatory indicators, and dietary status. Future causal studies should address these gaps. Future studies should incorporate biomarkers (inflammatory cytokines and oxidative stress) and psychological factors within a biopsychosocial continuum to account for this 43% of the variance, unexplained by this model. Further, implementation science research is needed to investigate what strategies are required to integrate routine fatigue screening into nephrology clinical and administrative processes, such as by using short validated measures, and evidence-based treatment algorithms.

Conclusion

This study confirms that most CKD patients experience moderate to severe fatigue, which worsens from mild to severe stages of CKD. Reduced eGFR, low haemoglobin, and high creatinine levels were the strongest independent predictors of fatigue together accounting for 57% of fatigue variance. Clinically, monitoring of fatigue, management of anemia, and kidney function should be part of the CKD treatment plan. Longitudinal and interventional studies are warranted in the future to prove causality and test targeted therapies for this debilitating symptom.

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Conflict of Interest

None

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None

Use of Artificial Intelligence

The corresponding author declared that no artificial intelligence or AI-assisted tools were used in this manuscript.

Authors' Contribution

MA, AR and MK contributed significantly and equally as per ICMJE. All authors gave their final approvals to publish this article.

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