

# Investigation of the effect of fibromyalgia frequency on quality of life, daily living activities, disease perception, and clinical parameters in patients with chronic kidney failure undergoing dialysis treatment

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## ABSTRACT

**Aims:** Fibromyalgia syndrome (FMS) may be under-recognized in hemodialysis populations, where chronic inflammation, musculoskeletal complaints, and reduced health-related quality of life (HRQoL) frequently overlap. This study evaluated the prevalence of FMS in hemodialysis and examined its associations with pain, activities of daily living, HRQoL, and routine dialysis/laboratory parameters.

**Methods:** In this cross-sectional study, 127 adults were analyzed: 69 patients receiving maintenance hemodialysis (dialysis group) and 58 non-dialysis patients with FMS diagnosed using the ACR 2011 criteria and the 2016 revision (FMS group). Within the dialysis cohort, participants were stratified as FMS(+) (n=38) and FMS(-) (n=31). Pain intensity was assessed using a 0–10 Visual Analog Scale (VAS), functional independence with Katz Activities of Daily Living (ADL), and HRQoL with SF-36 (domain scores and summary measures). Dialysis/laboratory variables included pre- and post-dialysis blood urea nitrogen (BUN), Kt/V, parathyroid hormone (PTH), sodium (Na), and calcium (Ca). The primary outcome was SF-36 Role Limitations-Emotional. Multivariable logistic regression (dialysis cohort) and ROC analyses were performed to evaluate predictors of FMS.

**Results:** The prevalence of FMS within the hemodialysis cohort was 55.1% (38/69). Between-group comparisons (dialysis vs FMS) showed higher BMI in the FMS group (28.7±4.8 vs 25.3±5.7; p<0.001), while VAS pain and Katz ADL scores were similar. SF-36 summary scores were higher in the FMS group (PCS, p=0.039; MCS, p=0.008; Total, p=0.012). At the domain level, General Health (45.1±16.1 vs 38.6±13.5; p=0.015) and Role Limitations-Emotional (62.0±40.2 vs 28.5±38.4; p<0.001) were higher in the FMS group. Within the dialysis cohort, Role Limitations-Emotional remained higher in FMS(+) patients (36.8±39.3 vs 18.2±35.3; p=0.024), and post-dialysis BUN was higher in FMS(+) patients (27.5±13.4 vs 19.8±4.3; p=0.008). In multivariable analysis, only post-dialysis BUN was independently associated with FMS (OR=1.10; 95% CI 1.02–1.19; p=0.012). Discrimination was moderate for post-dialysis BUN alone (AUC=0.684) and improved slightly with the multivariable model (AUC=0.726).

**Conclusion:** FMS was common among hemodialysis patients and was associated with differences in emotional role functioning and higher post-dialysis BUN. These findings support a multidimensional approach to screening in dialysis care that integrates symptom-based FMS assessment with HRQoL profiling and selected biochemical signals.

**Keywords:** Fibromyalgia, hemodialysis, chronic kidney disease, SF-36, activities of daily living, quality of life

## INTRODUCTION

FMS is a chronic condition characterized by widespread pain, fatigue, sleep disturbances, and cognitive dysfunction; it is more common in women and significantly reduces quality of life. It can occur alone or in conjunction with other pain syndromes and neuropsychiatric disorders.<sup>1</sup>

In pathophysiology, a bidirectional interaction between the nervous and immune systems is prominent; neuroinflammation is characterized by microglial activation and the release of proinflammatory mediators. These mediators engage with nociceptors and neurons, enhancing

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excitability and substantially augmenting pain processing pathways.<sup>2</sup>

The prevalence of FMS in the general population is reported to be between 0.5% and 6%; environmental, psychological, and genetic determinants are considered to contribute.<sup>3</sup> Chronic kidney disease (CKD) is closely associated with musculoskeletal disorders, and approximately two-thirds of hemodialysis patients develop musculoskeletal problems. The frequency of rheumatic findings increases with dialysis duration; therefore, the differential diagnosis of fibromyalgia should be carefully considered in this population. Current studies have yielded conflicting results regarding the prevalence of FMS in patients undergoing hemodialysis and peritoneal dialysis: some reports are similar to those in the general population, while others report higher frequencies.<sup>4</sup> FMS in peritoneal dialysis and kidney transplant patients may have similar prevalence rates to healthy individuals; the presence of FMS has been shown to be associated with more pronounced impairment in depressive symptoms, anxiety, and HRQoL in CKD.<sup>5</sup>

FMS diagnosis is challenging in hemodialysis patients; FMS should be considered if high inflammation parameters are present alongside widespread musculoskeletal pain. FMS pain often worsens with movement, reduces physical activity, and limits sun exposure, which increases the risk of osteoporosis and complicates the diagnosis and treatment of both bone mineral disorders and FMS.<sup>6</sup> Inflammatory biomarkers-neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), mean platelet volume (MPV), red blood cell distribution width (RDW), C-reactive protein (CRP), monocyte/lymphocyte ratio (MLR), CRP/albumin ratio, and lymphocyte/CRP ratio-have been investigated in the context of CKD and FMS.<sup>7</sup> Hemodialysis patients are known to be in a chronic inflammatory state; approximately half of patients with a GFR of 15-60 mL/min may have CRP>2.1 mg/dL. The uremic environment, decreased clearance, increased proinflammatory cytokines, oxidative stress, and acidosis, as well as acute/chronic stressors specific to the dialysis process, infection dynamics, dialysis water purity, and membrane compatibility, contribute to inflammation. Current evidence suggests that inflammation may be more pronounced in the FMS group undergoing hemodialysis.<sup>8</sup>

End-stage renal disease (ESRD) and dialysis care reduce HRQoL in physical, emotional, and social domains. The specific impact of FMS on HRQoL, activities of daily living, and routine clinical parameters in dialysis cohorts has not yet been comprehensively defined.<sup>9</sup> The heterogeneity in the literature regarding FMS prevalence and clinical/laboratory correlates may be attributed to differences in diagnostic criteria, sampling frameworks, and outcome selection.<sup>10-11</sup>

Therefore, studies evaluating rehabilitation-focused robust data on functionality (e.g., Katz Activities of Daily Living), HRQoL profiles (e.g., SF-36 components), and routine dialysis indicators (e.g., pre/post-dialysis BUN, Kt/V) together are needed. The current study aims to determine the prevalence of FMS in dialysis and to evaluate the relationships between FMS and pain intensity, Katz ADL, and SF-36 HRQoL, as well as laboratory and dialysis parameters. The hypothesis of this study is that the presence of FMS in hemodialysis patients negatively affects HRQoL and has a distinctive

profile associated with certain clinical-laboratory variables. The findings are intended to provide a basis for targeted assessment and rehabilitation approaches in dialysis follow-up.

## METHODS

### Ethics

The study was approved by the Ethics Committee of Kırıkkale University Faculty of Medicine (Date: 10.06.2021, Decision No: 2019.06.30). Informed consent was obtained from all participants. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

A total of 127 adult participants were included in this study. The sample consisted of two groups: (i) 69 patients undergoing hemodialysis due to chronic renal failure (dialysis group) and (ii) 58 patients diagnosed with FMS according to the 2011 criteria and 2016 revision of the American College of Rheumatology (ACR) 2011 criteria and 2016 revision and who were not receiving dialysis treatment (FMS group).

Inclusion criteria were being 18 years of age or older, meeting the relevant group's diagnostic/treatment criteria (being monitored in a hemodialysis program or having a diagnosis of FMS according to the 2016 revision of the ACR 2011 criteria), and providing written informed consent. Active infection, malignancy, advanced cognitive impairment, or severe psychiatric illness; concomitant rheumatologic disease (e.g., active inflammatory arthritis) or acute exacerbation; and lack of baseline data/scale scores required for the primary outcome analysis were defined as exclusion criteria.

Comparisons were planned on two axes. On the first axis, the dialysis group and the FMS group were compared as two independent cohorts. On the second axis, the dialysis cohort was analyzed by dividing it into FMS(+) (n=38) and FMS(-) (n=31) subgroups based on the presence of FMS according to the ACR 2011/2016 criteria.

The FMS diagnosis was evaluated according to the ACR 2011 criteria and the 2016 revision (Widespread Pain Index [WPI] and Symptom Severity Scale [SSS]). Pain intensity was measured on a 0-10 range using the Visual Analog Scale (VAS). Daily living activities were assessed using the Katz ADL (0-18); a higher score indicates greater independence, and the Turkish validity and reliability of the scale have been published. HRQoL was measured using the SF-36 (8 domains; 0-100; higher scores indicate better quality of life); additionally, the Physical Component Summary (PCS), Mental Component Summary (MCS), and the sum of the 8 domains were reported as the "Total" score. Demographic and sociodemographic data (age, gender, marital status, education, employment, smoking, etc.) were recorded. Body mass index (BMI, kg/m<sup>2</sup>) was calculated as an anthropometric measurement. In the dialysis group, routine laboratory/dialysis parameters (pre- and post-dialysis BUN, Kt/V, parathyroid hormone [PTH], sodium [Na], and calcium [Ca]) and dialysis-related clinical information were also evaluated.

The primary outcome was defined as the SF-36 "Role Emotional" domain score, focusing on rehabilitation-related emotional functioning. Secondary endpoints included SF-36

General Health, PCS, MCS, and Total scores; VAS, Katz GYA, and BMI; as well as dialysis/laboratory indicators (pre- and post-dialysis BUN, Kt/V, PTH, Na, and Ca).

Statistical analyses were performed using IBM SPSS 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean±SD or median (interquartile range) according to distribution; categorical variables were summarized as n (%). Normality was assessed using Shapiro–Wilk tests. For comparisons between the two groups, the independent samples t-test or Mann–Whitney U test was used for continuous variables, depending on the distribution; the chi-square test or Fisher’s exact test, when appropriate, was used for categorical variables. To evaluate factors associated with FMS within the dialysis cohort, a multivariate logistic regression model was constructed with the dependent variable “FMS present/absent,” and BUN output, PTH, Na, Ca, and Kt/V were included in the model; results were reported as odds ratio (OR), 95% confidence interval, and p-value. Discriminative performance in predicting FMS was evaluated using ROC analysis; threshold/classification criteria were reported based on AUC and the Youden index for univariate BUN output and multivariate models. For missing data, the complete data (listwise) approach was applied in primary/secondary analyses, and the two-tailed significance level was set at α=0.05.

## RESULTS

### Participants

A total of 127 participants were analyzed: 69 patients on hemodialysis and 58 fibromyalgia (FMS) patients not on dialysis; within the dialysis cohort, they were classified as FMS(+) n=38 and FMS(-) n=31 according to the ACR 2011/2016 criteria (Table 1).

**Table 1.** Baseline characteristics of dialysis and fibromyalgia groups (concise)

Characteristic	Dialysis (n=69)	Fibromyalgia (n=58)	p-value
Age, years (mean ± SD)	56.1±12.6	55.5±9.1	0.76
Female, n (%)	25 (36.2)	21 (36.2)	1.00
Married, n (%)	54 (78.3)	56 (96.6)	0.006
<b>Education, n (%)</b>			
≤Primary	50 (72.4)	15 (25.9)	
Secondary (middle)	11 (15.9)	15 (25.9)	
≥High school	8 (11.7)	28 (48.3)	<0.001 (overall)
Employed, n (%)	5 (7.2)	31 (53.4)	<0.001
Current smoker, n (%)	23 (33.3)	10 (17.2)	0.06
BMI, kg/m <sup>2</sup> (mean±SD)	25.3±5.7	28.7±4.8	<0.001
VAS pain (0–10)	5.54±2.49	6.02±1.67	0.33
Katz ADL (0–18)	16.7±2.9	16.9±1.9	0.14
SF-36 PCS (0–400)	159.8±79.3	176.1±60.0	0.039
SF-36 MCS (0–400)	186.8±75.8	219.8±72.6	0.008

Values are mean±SD or n (%). p-values from independent t-test or Mann-Whitney U test (continuous) and χ<sup>2</sup>/Fisher’s exact test (categorical), as appropriate. Education compared across three categories (overall p). PCS/MCS are SF-36 component summaries (higher=better). BMI: Body mass index, VAS: Visual Analog Scale, ADL: Activities of Daily Living, PCS: Physical Component Summary, MCS: Mental Component Summary

### Comparison of Dialysis and FMS Groups

Age was similar (56.1±12.6 vs. 55.5±9.1; p=0.76), and gender distribution was equal; the proportion of married individuals

was higher in the FMS group (96.6% vs. 78.3%; p=0.006) (Table 1).

BMI was higher in the FMS group (28.7±4.8 vs. 25.3±5.7; p<0.001); VAS (6.02±1.67 vs. 5.54±2.49; p=0.33) and Katz GYA (16.9 ± 1.9 vs. 16.7 ± 2.9; p=0.14) did not differ (Table 1).

In the SF-36 summaries, PCS (176.1±60.0 vs. 159.8±79.3; p=0.039), MCS (219.8±72.6 vs. 186.8±75.8; p=0.008), and Total (396.0±113.0 vs. 346.6±145.3; p=0.012) were higher in the FMS group (Table 1).

By domain, General Health (45.1±16.1 vs 38.6±13.5; p=0.015) and Role Limitations–Emotional (62.0±40.2 vs 28.5±38.4; p<0.001) favored FMS; there were no significant differences in other domains (Table 2).

**Table 2.** Health-related quality of life (sf-36) domain scores by group

SF-36 domain (0–100; higher=better)	Dialysis (n=69), mean±SD	Fibromyalgia (n=58), mean±SD	p-value (Mann-whitney U)
Physical functioning	42.8±29.3	52.4±21.5	0.061
Role physical	20.6±35.3	25.0±32.4	0.138
Bodily pain	57.6±19.7	53.6±15.1	0.332
General health	38.6±13.5	45.1±16.1	0.015
Vitality	44.8±18.2	43.4±17.2	0.658
Social functioning	54.1±24.6	59.0±21.6	0.227
Role emotional	28.5±38.4	62.0±40.2	<0.001
Mental health	59.3±17.7	55.3±12.5	0.182
SF-36 total (0–800)	346.6±145.3	396.0±113.0	0.012

Values are mean±SD. Higher scores indicate better health status. p-values from Mann-Whitney U test. To avoid redundancy with Table 1, VAS, Katz ADL, BMI, and SF-36 component summaries (PCS/MCS) are reported in Table 1. SD: Standard deviation

Within the dialysis cohort, FMS(+) and FMS(-) VAS (5.7±2.3 vs. 5.3±2.6; p=0.614) and Katz GYA (16.7±2.9 vs. 16.8±3.0; p=0.870) were similar; Role Limitations-Emotional was higher in the FMS(+) group (36.8±39.3 vs. 18.2±35.3; p=0.024), and the total score difference was not statistically significant (359.5±150.5 vs. 330.7±139.4; p=0.527) (Table 3).

Laboratory/dialysis indicators showed that BUN-output was higher in the FMS(+) group (27.5±13.4 vs 19.8±4.3; p=0.008); there were no differences in BUN-in (p=0.126), Kt/V (p=0.921), PTH, Na, and Ca (Table 3).

### Multivariate Analysis

In the logistic regression model established for the dialysis cohort (dependent variable: presence/absence of FMS), BUN output, PTH, Na, Ca, and Kt/V were included in the model together; only BUN output was independently associated with FMS (OR=1.10; 95% CI 1.02-1.19; p=0.012) (Table 4).

### ROC Analysis

AUC=0.684 was calculated for the univariate BUN-output model and AUC=0.726 for the multivariate model in predicting FMS; comparative curves were presented, and sensitivity/specificity values based on the Youden index for BUN-output were reported (Figure).

This study reveals the pattern of FMS comorbidity in dialysis patients on clinical and patient-centered outcomes using a comparative and multivariate approach. In between-group

**Table 3.** Dialysis cohort stratified by fibromyalgia (FMS): clinical outcomes and key laboratory indices

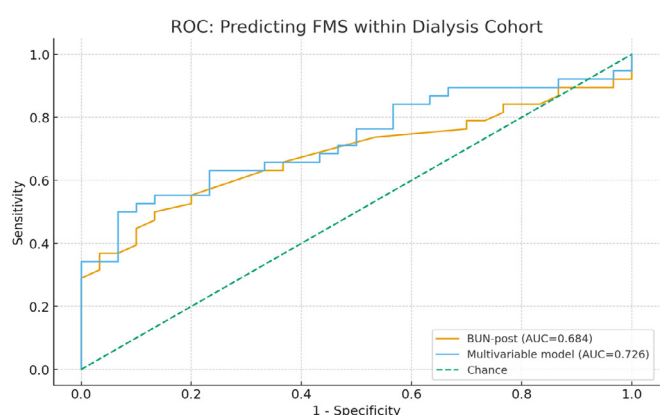
Outcome	Dialysis+FMS (n=38), mean±SD	Dialysis without FMS (n=31), mean±SD	Mean diff.	Test	p-value
VAS pain (0–10)	5.7±2.3	5.3±2.6	+0.4	MWU	0.614
Katz ADL (0–18)	16.7±2.9	16.8±3.0	-0.1	MWU	0.870
SF-36 role emotional (0-100)	36.8±39.3	18.2±35.3	+18.6	MWU	0.024
SF-36 total (0–800)	359.5±150.5	330.7±139.4	+28.8	MWU	0.527
BMI (kg/m <sup>2</sup> )	25.2±6.1	25.4±5.1	-0.2	MWU	0.495
BUN pre-dialysis (mg/dl)	75.1±19.9	69.1±11.7	+6.0	t-test	0.126
BUN post-dialysis (mg/dl)	27.5±13.4	19.8±4.3	+7.7	MWU	0.008
Kt/V	1.30±0.34	1.34±0.33	-0.04	MWU	0.921

Values are mean±SD. Mean diff.=(FMS+)-(FMS-). MWU: Mann-Whitney U. Higher scores indicate better status for SF-36 scales. To minimize redundancy, additional domains and labs are provided in Supplementary Table S1. FMS: Fibromyalgia syndrome, VAS: Visual Analog Scale, ADL: Activities of Daily Living, BMI: Body mass index, BUN: Blood urea nitrogen

**Table 4.** Multivariable logistic regression within dialysis cohort (outcome: FMS)

Predictor	OR (95% CI)	p-value
BUN post-dialysis	1.10 (1.02-1.19)	0.012
PTH	1.00 (1.00-1.00)	0.162
Na	0.99 (0.94-1.03)	0.589
Ca	1.02 (0.56-1.84)	0.954
KT_V	0.64 (0.12-3.44)	0.604

Multivariable logistic regression within dialysis cohort (outcome: FMS). Predictors entered: BUN post-dialysis (mg/dl), PTH (pg/ml), Sodium (mmol/L), Calcium (mg/dl), Kt/V. Results reported as odds ratios (OR) with 95% confidence intervals and p-values. FMS: Fibromyalgia syndrome, BUN: Blood urea nitrogen, PTH: parathyroid hormone, Na: Sodium, Ca: Calcium



**Figure.** ROC curves predicting fms within the dialysis cohort

Univariate BUN post-dialysis vs multivariable model (BUN-post, PTH, Na, Ca, Kt/V). AUC values are shown in the legend of the plot.

analyses, BMI was found to be higher in FMS patients; SF-36 summary scores (PCS, MCS) and total score favored FMS; and at the domain level, general health and role limitations–emotional dimensions were found to be particularly higher (Table 1, Table 2). When looking at the dialysis cohort itself, the Role Limitations–Emotional score was higher in the FMS(+) subgroup; among laboratory indicators, the BUN-output level was significantly higher in FMS(+) cases (Table 3).

Multivariate modeling revealed that BUN output in dialysis patients showed an independent relationship with FMS (OR≈1.10). This finding strengthens hypotheses suggesting that the FMS phenotype may be associated with persistent post-dialysis urea/solute load, metabolic stress, or inflammation/catabolism. However, indicators such as PTH, Na, Ca, and Kt/V did not show an independent relationship; this situation is shown in Table 4.

In the discriminatory performance analysis, BUN-output alone presented a moderate AUC, while the AUC

of the multivariate model including BUN-output+PTH/Na/Ca/Kt/V was relatively higher. This table suggests that, in clinical practice, a multidimensional assessment (biochemistry+clinical/functional measurements) approach may be more rational than screening with a single biomarker (Figure).

Two implications of the findings stand out in terms of rehabilitation. First, in dialysis patients, FMS screening (symptom inquiry, WPI/SSS-based assessment) should be considered together with HRQoL profiling (especially emotional role functioning). Second, in cases where elevated BUN output is detected, the presence of accompanying FMS should be considered, and a multidisciplinary approach (nephrology–physical therapy/rehabilitation–psychosocial support–pain management) can be planned, thus enabling more selective application of targeted exercise prescriptions, behavioral strategies, and pharmacological interventions if necessary (Table 3, Table 4 and Figure).

The findings of this study suggest that FMS may constitute a significant comorbidity in the dialysis population, affecting not only “increased pain” but also emotional role functioning and overall health perception. Furthermore, the presence of biological burden (BUN-output) associated with post-dialysis urea clearance in this phenotype may add a perspective that incorporates a metabolic/solute kinetics component to the biopsychosocial framework of FMS (Table 2, Table 4).

## DISCUSSION

Our study found that the presence of fibromyalgia was associated with higher scores on the primary outcome measure, SF-36 “Role Limitations-Emotional,” both when comparing the two independent groups and within the dialysis cohort alone. Although this finding may initially appear to contradict the expectation of “decreased emotional and social functioning” in the fibromyalgia literature, it presents a meaningful picture when sample characteristics and contextual factors are considered: Higher rates of employment/marriage in the fibromyalgia group, the absence of multiple biological stressors associated with chronic kidney failure and hemodialysis, and similar levels of pain intensity between groups may explain the relative preservation of emotional role functioning. In short, the emotional role domain here may reflect a relative advantage compared to the global burdens of dialysis (fatigue, treatment regimen, comorbidities, time constraints) rather than a “fibromyalgia-specific limitation.”

Second, the absence of significant differences in pain (VAS) and functional independence (Katz GYA) measures suggests that the divergence in emotional role scores cannot be explained solely by pain intensity. This situation implies that cognitive-emotional processes shaping the pain experience in fibromyalgia (coping styles, expectations, self-efficacy, social support) and the “treatment-imposed lifestyle” in dialysis may produce different effects on emotional functioning.<sup>12</sup> In other words, while the total pain burden appears similar in both conditions, its reflection on role performance may be context-sensitive.

In a multivariate analysis within the dialysis cohort, post-dialysis BUN level showed an independent association with fibromyalgia. The lack of significance for Kt/V, PTH, sodium, and calcium suggests that classic “dialysis adequacy” parameters are not independently associated; however, the post-session residual solute load (or the metabolic/catabolic processes representing it) may be more closely associated with the fibromyalgia phenotype.<sup>13</sup> This relationship raises several possible mechanisms: (i) the effects of residual uremic toxins on central sensitivity and sleep ecology, (ii) inflammation-related neuromodulatory responses, and (iii) indirect effects on affect and role performance via post-session fatigue/exhaustion.<sup>14</sup> In the discriminant performance analysis, the fact that BUN-output alone showed moderate discriminant power, while the multivariate model showed slightly higher discriminant power, suggests that it is more realistic to consider biological and psychosocial signals together rather than a single biomarker in clinical practice.

Indicators such as PTH, Na, Ca, and Kt/V did not show an independent relationship; this is not surprising given the biopsychosocial nature of FMS and its relationship with pain neuromodulation processes.<sup>15</sup> CKD-MBD variables (PTH, Ca) may relate more to bone pain, cramps, or neuropathic phenotypes than to an FMS-defined central sensitivity syndrome; null findings here may reflect limited power, treatment effects (e.g., phosphate binders/vitamin D), or the need for more granular pain phenotyping (neuropathic vs nociplastic).<sup>16,17</sup>

The pattern obtained conveys three messages for rehabilitation practices: First, when screening for fibromyalgia in dialysis patients, the systematic assessment of emotional role functioning is as important as pain intensity; this domain may differ from expectations and alter intervention targets.<sup>18</sup> Second, monitoring post-session metabolic load (e.g., BUN-output trend) may provide clinicians with additional warning regarding fibromyalgia risk or severity; it is not diagnostic on its own but may trigger a multi-faceted assessment.<sup>19,20</sup> Third, comprehensive protocols (individualized exercise, sleep hygiene, behavioral strategies, pain education, and pharmacotherapy when indicated) for planned interventions should be designed in sync with dialysis session timing and fatigue patterns.<sup>21</sup>

The findings reframe the heterogeneous reports in the literature: HRQoL losses attributed to fibromyalgia can be broken down into different components in the dialysis context; the expected “decrease” in the emotional role domain may not always be observed.<sup>22</sup> This can be explained by sample selection (type of clinical referral, being under active treatment/supervision), sociodemographic profile, and level

of social support. Additionally, differences in cultural factors and the sustainability of work/family roles may particularly affect emotional role scores.<sup>23</sup> Cross-cultural measurement studies also suggest that the SF-36 Role Emotional domain may behave differently across regions, partly because some respondents are less inclined to attribute role limitations to emotional states, which can shift observed scores independent of symptom severity.<sup>24</sup> In addition, international dialysis cohort data and qualitative research describe systematic cross-national differences and “response shift” phenomena in HRQoL appraisal, indicating that emotional role scores may be shaped by cultural norms and adaptation processes beyond biomedical determinants.<sup>25,26</sup>

Conceptually, fibromyalgia is a prototypical nociplastic pain condition, and dialysis-related pain often reflects a mixture of nociceptive, neuropathic, and nociplastic mechanisms. Recognizing and phenotyping this mix may improve rehabilitation targeting (exercise, sleep, psychological strategies) and reduce over-reliance on analgesics in a population where medication harm is a real constraint.

Limitations include the cross-sectional design (no causal interpretation possible), single-center sample (limited generalizability), failure to model all psychosocial co-determinants (mediators/confounders such as anxiety, depression, and sleep disorders), and the nature of self-report scales. Multiple field tests may increase the risk of type I error; however, the primary endpoint was predefined, and the results were interpreted within a hypothesis-generating framework. Strengths include the two-axis comparison design (independent cohort+dialysis subgroups), the joint reporting of biological and psychosocial measures, and the support of findings by multivariate/discriminant analyses.

In conclusion, this study suggests that fibromyalgia may affect emotional role functioning in a “different than expected” way in the dialysis context and that post-dialysis solute load may be associated with the fibromyalgia phenotype. In clinical practice, screening and intervention plans should be designed to be sensitive not only to pain intensity but also to emotional role performance and post-session biological load. Furthermore, prospective, multicenter studies should be conducted to elucidate metabolic-neuromodulatory interactions.

### Limitations

The cross-sectional nature of the design limits causal inferences; the direction/intermediate mechanisms of the FMS and BUN-output relationship should be investigated in prospective studies. The single-center sample and sample size (particularly degrees of freedom in multivariate models) may limit generalizability. Psychosocial variables (anxiety, depression, and sleep quality) were not included in the model; these may play mediating/confounding roles. Finally, there is a risk of type-I error in the multiple comparisons of SF-36 domains; however, the primary outcome of the study was pre-specified, and findings are presented in a hypothesis-testing manner (Table 1, Table 4).

Strengths include the fact that FMS was addressed in the dialysis context with both HRQoL and clinical and laboratory indicators and structured tables; furthermore, a predictive framework for clinical applicability was presented using

logistic regression and ROC analyses. This approach may help rationalize screening/monitoring strategies in the field (Table 3, Table 4 and Figure).

## CONCLUSION

The independent relationship between BUN-output and FMS in the dialysis cohort indicates the intersection of biological burden and pain/emotional functioning in rehabilitation-focused care. In clinical practice, considering post-dialysis solute load alongside FMS screening and HRQoL profiling may facilitate targeted interventions. Prospective and multicenter studies are needed to elucidate the causal pathways, metabolic and neuromodulatory mechanisms, and intervention response of these findings (Table 4 and Figure).

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was approved by the Ethics Committee of Kırıkkale University Faculty of Medicine (Date: 10.06.2021, Decision No: 2019.06.30).

### Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights-including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

### Peer Review Process

This manuscript was subject to external peer review.

### Conflict of Interest

The authors declare no conflicts of interest related to this study.

### Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

### Author Contributions

Concept: T.K., A.Ç.; Design: T.K., A.Ç., H.Ö.; Control: T.K., A.V., A.Ç.; Data collection and/or processing: T.K., Z.C., H.Ö., A.Ç.; Analysis and/or interpretation: T.K., A.V., Z.N.Ö., Z.C.; Literature review: T.K., Z.C., A.V., A.Ç.; Article writing: T.K., A.V., Z.N.Ö., Z.C., A.Ç.; Critical review: All authors.

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