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ORIGINAL ARTICLE

Fibromyalgia Prevalence and its Association with Laboratory Parameters in Patients with Chronic Renal Failure

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ABSTRACT

Backround: This study aimed to evaluate the prevalence of fibromyalgia syndrome in patients with chronic renal failure and evaluate the association of this syndrome with gender, age, hemodialysis , and laboratory parameters.
Patients and Method: The study was designed as cross-sectional prospective clinical study. A total of 135 patients with chronic renal failure were included in the study; 65 of the patients participating in the study were randomly selected from the ones who were diagnosed with grade 3–4 chronic renal failure and were under clinical follow-up.
Results: Of the 135 patients who participated in the study, 74 (55.8%) were female and 61 (45.2%) were male. Eighteen of the seventy (25.7%) patients who were diagnosed with fibromyalgia syndrome were in the hemodialysis group and 12/65 (18.4%) were in the predialysis group. The Fibromyalgia impact questionnaire result was 66.2 ± 15.01 in the dialysis group (N = 18) and 65.45 ± 4.17 in the predialysis group (N = 12). In the predialysis group, low vitamin D (p= 0.000), high acute-phase reactant (p= 0.00) and high uric acid levels (p=0,001) were detected. Statistically significant high thyroid-stimulating hormone and aspartate aminotransferase values were found with the presence of fibromyalgia syndrome in both the groups. The logistic regression analysis (analysis of variance) revealed that vitamin D had a high predictive value for the presence of fibromyalgia syndrome in the predialysis group (beta = 0.42, p= 0.001, confidence interval 0.41).
Conclusion: Systemic disorders such as hypothyroidism, vitamin D deficiency, and inflammation may also contribute to the development of fibromyalgia syndrome in chronic renal failure patients.

Keywords: Fibromyalgia, chronic renal failure, hemodialysis cystosarcoma phyllodes

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INTRODUCTION

Fibromyalgia syndrome (FMS) is a condition characterized by high levels of pain, sleep disturbance, and fatigue combined with a general increase in memory disturbances leading to psychological distress (1). It negatively affects life quality and has not been studied well in specific patient populations.
Chronic renal failure (CRF) may be associated with FMS due to symptoms such as pain and sleep disturbance, insomnia, depression, anxiety, and restless legs syndrome. A small number of clinical trials have evaluated the relationship between FMS prevalence and laboratory parameters in CRF or hemodialysis (HD) patients [1].
The objective of this study was to evaluate the prevalence of FMS in patients with CRF and evaluate the association of this syndrome with gender, age, HD, and laboratory parameters

MATERIAL and METHOD

A total of 135 (74 female/61 male) patients with CRF were included in this study; 65 of the patients

participating in the study were randomly selected from the ones who were diagnosed with stages 3–4 CRF and were under a clinical follow-up (predialysis group). Seventy of these patients were selected from the ones who had CRF and had been undergoing HD at a hemodialysis clinic at a Research and Training Hospital twice a week. The age, gender, body mass index (BMI), HD duration, comorbid systemic disease, Visual analog scale (VAS) for pain, and laboratory parameters of each participant were recorded. Each patient was questioned for FMS-related symptoms and diagnosed based on American College of Rheumatology 2010 criteria. In all patients, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), 25'(OH) vitamin D, parathyroid hormone (PTH), calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), aspartate aminotransferase (AST), and thyroid-stimulating hormone (TSH) values were recorded. Moreover, patients who were diagnosed with FMS were asked to fill in the Fibromyalgia Impact Questionnaire (FIQ).

FIQ score means low under 25, below average between 26-50, average to high between 50-69 and severe higher than 70. The higher your total score, the more impact fibromyalgia is having on your life. IBM SPSS 21.0 for Windows (IBM Corp., NY, USA) statistical package program was used for evaluating the data. Explanatory statistics of the study were shown as mean± standard deviation for continuous data, and categorical variables were also shown as frequency and percentage. Data suitability of the normal distribution was analyzed by the Kolmogorov Smirnov test, and the homogeneous distribution of variances was also evaluated by histograms. Nominal demographic data of the patients were compared using the chi-square test. Normal distribution was assessed using the t test, and the Mann–Whitney U test was used for non-normal distribution. For predictive analysis, we used the logistic regression test. A P value less than 0.05 was considered statistically significant.

RESULTS

Of the 135 patients who participated in the study, 74 (55.8%) were female and 61 (45.2%) were male. Age distribution was 59.5 ± 13.1 years in the dialysis group and 51.5 ± 10.9 years in the predialysis group.
The distribution of FMS patients in both groups are shown in Table 1.

Table 1. Prevalence of FMS in predialysis and dialysis groups

Group	FMS presence (N,%) Yes	FMS presence (N,%) No
Dialysis	18/25.7%	52/74.3%
Predialysis	12/18.4%	53/81.6%
Total	30/22.2%	105/77.8%

Abreviations: FMS: Fibromyalgia syndrome

Eighteen of the seventy (25.7%) patients who were diagnosed with FMS were in the HD group and 12/65 (18.4%) were in the predialysis group. The FIQ result was 66.2 ± 15.01 in the dialysis group (N = 18) and 65.45 ± 4.17 in the predialysis group (N = 12), with no statistically significant difference (P= 0.80). Further, 48.6% of the patients had been undergoing dialysis for 5 or more years (Table 2).

Table 2. Percentage distribution of dialysis time

Time	<1 year	1-3 year	3–5 years	>5 years
Dialysis group (N,%) Total, N= 70	14/20%	19/27.1%	3/4.3%	34/48.6%

All parameters for both the groups are given in Table 3.

Table 3. Comparison of study data in the predialysis and dialysis groups

	Dialysis group	Predialysis group
Age (year)	59.52±13.1	51.56±10.98
BMI (kg/m^2)	24.19±4.17	27.63±2.5
VAS (cm)	3.88±3.34	6.24±1.66
ESR (mm/h)	58.33±30.42	22.43±9.42
CRP (mgr/L)	1.04±1.47	1.84±1.37
Vit D (ng/mL)	16.88±9.57	14.43±7.64
PTH (pg/mL)	543.26±553.5	85.38±57.9
Ca (mg/dL)	8.47±0.73	8.64±0.59
Urıc acid (mg/dL)	6.58±1.02	5.30±1.41
AST (U/L)	15.27±11.4	19.26±7.74
P (mg/dL)	5.63±1.31	4.53±0.83
TSH (µU/ml)	1.98±1.47	2.80±1.19
ALP (U/L)	187.34±206.7	75.36±27.26
FIQ	66.29±15.01	65.45±4.17

Abbreviations: BMI: Body mass index; VAS: Visual analog scale; ESR: Erythrocyte sedimentation rate CRP: C-reactive protein; PTH: Parathyroid hormone; ALP: Alkalene phosphatase; AST: Aspartate aminotransferase FIQ: Fibromyalgia impact questionnaire; TSH: Thyroid stimulant hormone

As a result, vitamin D level in both the groups were 16.8 ± 9.5 ng/mL (20–30 ng/mL) in HD and 14.4 ± 7.6 ng/mL (20–30 ng/mL) in the predialysis group.

When both groups were compared in terms of all parameters, BMI, VAS, TSH, and AST were found to be high in the predialysis group, whereas ESR, CRP, PTH, ALP, and P were high in the dialysis group. No significant differences in vitamin D, FMS presence, FIQ, and Ca values were observed between groups.

When the predialysis group was divided into two groups according to the presence of FMS, significant differences were found in several parameters such as VAS (p= 0,000), ESR (p= 0,000), CRP (p= 0,001), vitamin D (p= 0.001), TSH (p= 0.37), and uric acid (P= 0.001). VAS, ESR, CRP, ALP, P, uric acid, and TSH values were high in the FMS group, but the vitamin D level was significantly low (Table 4 and Figure 1).

Table 4. Comparison of study data in predialysis patients according to the presence of FMS

	FMS, yes (mean±std)	FMS, no (mean±std)
Age (year)	52.72±10	50.97±11.5
BMI (kg/m^2)	28.61±2.43	27.13±2.42
VAS (cm)	7.77±0.61	5.46±1.48
ESR (mm/h)	28.86±7.27	19.13±8.72
CRP (mg/L)	2.65±1.59	1.43±1.06
Vit D (ng/mL)	8.87±3.70	17.27±7.6
PTH (pg/mL)	102.09±41.6	76.83±63.41
Ca (mg/dL)	8.62±0.71	8.65±0.52
P (mg/dL)	4.94±0.57	4.32±0.86
ALP (U/L)	90.45±25.96	67.65±24.8
Uric acid (mg/dL)	6.09±1.2	4.89±1.34
AST (U/L)	20.59±7.18	18.58±8.01
FIQ	65.45±4.17	
TSH (µU/ml)	2.91±1.16	2.74±1.22

Abbreviations: FMS: Fibromyalgia syndrome; BMI: Body mass index; VAS: Visual analog scale; ESR: Erythrocyte sedimentation rate CRP: C-reactive protein; PTH: Parathyroid hormone; ALP: Alkalene phosphatase; AST: Aspartate aminotransferase

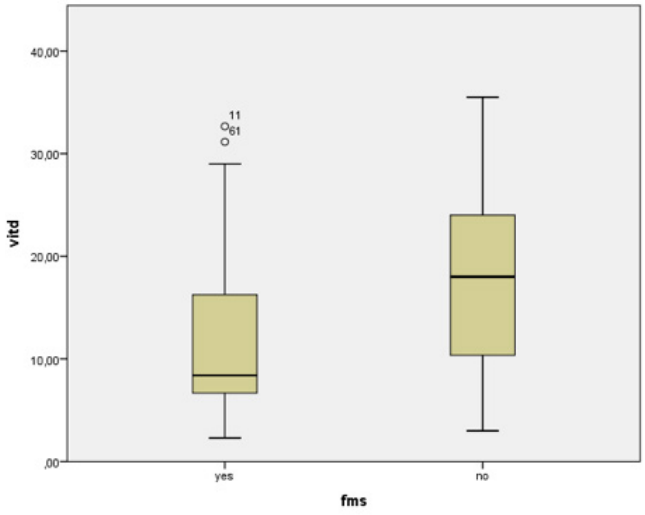

Figure 1. FMS prevalence and vitamin D level distribution graph in the predialysis group.

The logistic regression analysis revealed that the vitamin D level in the predialysis group had a high predictive value for the presence of FMS (beta = 0.42, p= 0.001; confidence interval 0.41). VAS (p= 0.000), AST (p= 0.004), and TSH (P= 0.040) values were significantly high in the FMS group when the dialysis group was evaluated for FMS presence. Vitamin D, PTH, and other parameters were not significantly different.

DISCUSSION

FMS is a chronic pain syndrome mainly affecting females. It is a major health issue because its prevalence is high (around 2%) and it has a large impact on life quality in patients [1, 2]. Moreover, it is still a controversial disease owing to disputes concerning its etiology, pathogenesis, and classification.

The relationship between pain and psychiatric disorders, as well as sleep disorders, is complex and bidirectional in FMS. Distress and sleep disorders can either be a cause or a consequence of pain [3]. Individuals with chronic systemic disease complain about having shorter and restless sleep compared with healthy people. These sleep disorders worsen the subjective symptoms of FMS.

CRF may cause sleep disturbances such as insomnia, insufficient sleep, sleep apnea, or restless legs syndrome. Sleep disturbance increases the pain sensation and reduces the life quality. In particular, accompanying psychiatric comorbidities (depression and anxiety) also contribute to the sleep disturbance. A number of common complaints are similar to FMS symptoms in CRF patients [4,5].

CRF is an important health problem worldwide. Its treatment causes a heavy burden on patients and their families. Daily life limitations can worsen the situation and affect the life quality [6]. The combination of CRF and HD with FMS has been the subject of research. The presence of FMS may worsen life quality in patients with this combination. Therefore, patients with CRF should be carefully examined for accompanying FMS symptoms, and the underlying causes should be investigated [7,8].

Leblebici et al. found that the prevalence of FMS in Turkish HD patients was 9% (higher than the normal population) [7]. They also found an association between this prevalence and several other factors such as sleep disturbance, fatigue, education level, and cognitive symptoms. They did not find any difference in laboratory parameters. Yucetürk et al9. and Couto et al. [10] showed that the FMS prevalence in HD patients was similar to that in the general population. They also reported that no laboratory parameters were correlated with FMS frequency. The study by Samimmaqham et al. showed that FMS was correlated with sleep deprivation and depression in HD patients more than that in the normal population [11].

The FMS prevalence in the present study was high compared with that of the normal population. Low vitamin D and high acute-phase reactant levels in the predialysis group and high TSH values in both two groups were associated with the presence of FMS due to laboratory parameters.

Low calciferol level and FMS are the two most common concerns in recent years, and both cause chronic pain. Other than pain complaints, vitamin D levels can also affect the FMS symptoms such as anxiety, depression, and sleep disturbances. Highly frequent and long-term generalized muscle and bone pain are associated with low 25(OH) vitamin D levels, and these cases can often be diagnosed with FMS. Cholecalciferol deficiency has been shown to be associated with sleep–wake disorder. Increased pain rate was associated with sleep deficiency and interleukin-6, an inflammatory marker that is known to increase in people with 25(OH) vitamin D deficiency [1].

Recent evidence supports that FMS may be associated with inflammation and endothelial dysfunction [12]. Chilcot et al.13 observed a modest correlation between elevated CRP levels and depressive symptoms in HD patients. ESR and CRP values were

significantly higher in the HD group in the present study. Also, a significant association was found between the presence of FMS and acute phase reactants in the predialysis group. Therefore, it is inferred that high inflammation increases the prevalence of FMS. The mechanisms underlying the association between FMS and inflammation may be the subject of future investigation.

Many clinical studies have demonstrated the association between autoimmune thyroid disease with FMS. Autoimmune thyroid disease has been shown to cause widespread pain through inflammatory mediators, small-fiber polyneuropathy, and central sensitization. FMS-like symptoms can also be seen in hypothyroidism [14,15]. A significant correlation was found between hypothyroidism (high TSH) and the presence of FMS in both the HD and predialysis group in the present study. This might be due to the similar clinical symptoms and concomitant disease.

Although no significant association between FMS and PTH was found in the present study, it should not be forgotten that hyperparathyroidism may also cause FMS-like symptoms [16,17]. It is thought that individuals with hyperparathyroidism or hypothyroidism in this study might have been misdiagnosed with FMS due to similar clinical symptoms. Moreover, uric acid and AST elevation were also significantly associated with the presence of FMS in the predialysis group.

Fatigue is a common symptom of end-stage renal failure [18]. Chronic fatigue in FMS is one of the most common complaints due to restless sleep. Somatic symptoms are also common in HD patients. Their causes are often unknown, and the treatment is unsuccessful [19]. The study by Barret et al. [20] aimed to establish a relationship between psychological and clinical factors. It showed a significant association of each somatic symptom with affection and life quality. Fatigue, itching, sleep disturbance, and cramps were found to be strongly associated with poor affection scores. Physical and mental parameters in dialysis patients were also associated with PTH level, duration of dialysis, task-coping, and working status [21].

CONCLUSION

CRF is a disease that negatively affects life quality. CRF patients usually have a close relation with FMS symptoms such as pain, chronic fatigue, sleep disturbance, psychiatric comorbidities (depression and anxiety), and restless legs syndrome. Moreover, various systemic disorders such as hypothyroidism, vitamin D deficiency, and inflammation may also contribute to the development of FMS. Therefore, nephrologists should consider the possibility of FMS in CRF patients.

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