PREVALENCE OF FIBROMYALGIA SYNDROME AND ITS EFFECT ON QUALITY OF LIFE IN HEMODIALYSIS PATIENTS

HEMODİYALİZ HASTALARINDA FİBROMİYALJİ SENDROMU PREVALANSI VE YAŞAM KALİTESİNİ ETKİSİ

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Abstract

Objective: We evaluated the prevalence of fibromyalgia syndrome (FM) in hemodialysis patients and whether this syndrome was associated with gender, age, duration of hemodialysis, or other laboratory parameters.

Methods: The study included 248 patients with chronic kidney disease (CKD) undergoing hemodialysis. The patients were stratified into two groups: patients with FM based on the 2010 American College of Rheumatology diagnostic criteria and patients not meeting these criteria without FM. Quality of life (QOL) was assessed using the Short Form-36 (SF-36) and Kidney Disease Quality of Life-36 (KDQOL-36) questionnaires. Sociodemographic data, laboratory parameters, and a marker for adequacy of hemodialysis (Kt/V) were recorded.

Results: FM was detected in 33/248 (13.3%) of patients included. All patients diagnosed as FM were female. When all sub-parameters of SF-36 and KDQOL-36 were compared, QOL was lower in the FM group compared to patients without FM (p<0.05). When laboratory parameters, dialysis duration, Kt/V, marital status and BMI were compared, no difference was detected between groups (p>0.05). FM frequency was higher in cases of advanced age, presence of systemic disease and/or hepatitis B and C infection in patients undergoing hemodialysis (p<0.05). In addition, FM frequency was inversely proportional to education level (p<0.05).

Conclusion: FM, associated with a significant decrease in QOL, is more commonly seen in CKD patients undergoing dialysis compared to the general population. Thus, it will be helpful to keep FM in mind and to improve QOL in these patients by early diagnosis and treatment.

Keywords: Hemodialysis, fibromyalgia syndrome, prevalence, quality of life

Öz

Amaç: Bu çalışmada, hemodiyaliz hastalarında fibromiyalji sendromu (FM) prevalansını ve bu sendromun cinsiyeti, yaş, hemodiyaliz süresi veya diğer laboratuvar parametreleri ile ilişkili olup olmadığını değerlendirildik.

Yöntem: Çalışmaya katılan bireylerin 33’ünde (%13,3) FM sendromu saptandı. FM tanısı alan tüm hastaların hepsi kadın cinsiyetliydi. FN, 2010 Amerikan Rayumoloji Derneği (ACR) tanım kriterlerine göre FM olan hastaların %33’ü FM sendromu saptandı.

Sonuç: FM prevalansı cinsiyet, yaş, hemodiyaliz süresi ve laboratuvar verileri ile ilişkili olup olmadığını değerlendirildi. FM prevalansı cinsiyeti, yaş, hemodiyaliz süresi ve laboratuvar verileri ile ilişkili olup olmadığını değerlendirildi. FM prevalansı cinsiyet, yaş, hemodiyaliz süresi ve laboratuvar verileri ile ilişkili olup olmadığını değerlendirildi. FM prevalansı cinsiyet, yaş, hemodiyaliz süresi ve laboratuvar verileri ile ilişkili olup olmadığını değerlendirildi. FM prevalansı cinsiyet, yaş, hemodiyaliz süresi ve laboratuvar verileri ile ilişkili olup olmadığını değerlendirildi.
Introduction

Fibromyalgia (FM) syndrome is a nonarticular rheumatic disease characterized by chronic diffuse musculoskeletal pain. Common body pain in patients is accompanied by signs and symptoms such as morning stiffness, headache, irritable bowel and bladder disease, anxiety, depression, Raynaud's phenomenon, dry eye, dry mouth, sleep disorders, swelling of hands, and paresthesia. The etiology and pathophysiology of FM are not known, but genetic, psychological, and environmental factors and peripheral and central mechanisms have been suggested as possible causes.

The prevalence of FM is reported to be between 2-8%. The prevalence of FM in females in the 20-64 age group was found to be 3.6% in a screening study conducted in Turkey. Although FM is seen in all ethnic groups of all ages and genders, it most frequently affects women in the 40-60 age group.

Chronic kidney disease (CKD) is defined as a condition where objective kidney damage and/or glomerular filtration rate (GFR) of at least three months standing is less than 60 ml/min/1.73 m², regardless of the underlying etiology of renal disease. Evidence of kidney damage may be of a structural or functional nature; these findings can be obtained from urine, blood tests, imaging studies and/or renal biopsy.

There are a limited number of studies into FM in specific populations. Some of these studies have focused on rheumatic symptoms in kidney patients. Rheumatologic diseases are major complications of CKD and approximately 60% of hemodialysis patients develop musculoskeletal disease. However, few studies have investigated the frequency of FM in individuals with CKD.

This study aimed to evaluate the incidence of FM in hemodialysis (HD) patients and the effect of FM on quality of life in these patients. A further aim of the study was to examine the relationship between FM and routine laboratory results and Kt/V values, which are indicators of dialysis adequacy in CKD patients.

Methods

This was a cross-sectional study. It was approved by Cumhuriyet University Ethics Committee (Project Number 2016-01/22). The study protocol was prepared in accordance with the Helsinki Declaration. Participation in the study was voluntary. Written, informed consent was obtained from all patients before their participation. No, a priori sample size calculation was conducted. The sample size was based on the available population of patients.

Participants

In this study, 383 patients over 18 years of age receiving hemodialysis treatment were interviewed between April 2016 and July 2016 from five centers: 1) Cumhuriyet University Medical Faculty Hospital, Nephrology Clinic Hemodialysis Unit; 2) Sivas Numune Hospital Hemodialysis Unit; 3) Private Sivas Dialysis Center, 4) Sivas Diaverum Central Anatolian Special Dialysis Center; and 5) Sivas Medicana Hospital Hemodialysis Unit. The inclusion criteria were as follows: 1) Routine hemodialysis treatment for at least three months, three times a week for CKD; 2) aged >18 years old; and 3) giving fully informed, competent consent for the study. The exclusion criteria were as follows: 1) Hemodialysis treatment for less than three months and less than three sessions per week due to CKD; 2) any malignancy; 3) rheumatologic disease including rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, familial Mediterranean fever; and 4) orthopedic problems, sequelae of cerebrovascular disease or neuromuscular disease that limit mobilization.

Volunteers who agreed to take part in the study underwent an interview and physical and clinical evaluation, and completed the questionnaires at the same session. All individuals included in the study were evaluated in detail in terms of FM diagnosis according to ACR 2010 diagnostic criteria, which occurred when the widespread pain index (WPI) was ≥7 and the symptom severity (SS) scale score was ≥5, or when the WPI was between 3 and 6 and the SS scale score was ≥9. In addition, the patients’ symptoms needed to have been of this severity for at least three months, and there was no other disorder that could have caused the pain.

Thirty-three patients (39 females) met the 2010 ACR criteria for FM Syndrome. The control group consisted of 215 patients (100 females, 115 males) who also had CKD but were not diagnosed with FM, based on ACR criteria.

Kidney Disease Quality of Life-36 (KDQOL-36) and Short Form-36 (SF-36) questionnaires were completed by all subjects to evaluate their QOL. In addition, the Fibromyalgia Impact Questionnaire (FQ), which is specific for FM patients, was administered to individuals diagnosed with FM to assess their current health status. Questionnaires were administered to all subjects by the same researcher through face-to-face interviews. In addition, the results of the routine clinical and laboratory examinations performed in the previous month were recorded. These parameters included body mass index (BMI), hemoglobin, blood urea nitrogen (BUN), creatinine, albumin, alkaline phosphatase (ALP), Calcium and Phosphate (Ca, P), parathyroid hormone (PTH) and Kt/V values.

Statistical analyses were performed using the SPSS for Windows version 22.0 software program (IBM Inc., Chicago, IL, USA). The Kolmogorov-Smirnov Z test was used in order to test whether parametric test assumptions were fulfilled or not. When parametric test assumptions were not fulfilled, Mann Whitney-U test was used for two-category variables and Kruskal Wallis H test was used for variables with more than two categories. When parametric test assumptions were fulfilled, the Independent Sample t-Test was used for two categorical variables and the F Test was used for more than two categorical variables. In addition, the Chi-Square test was used to compare if both variables were categorized. A p<0.05 was considered to be statistically significant.

Results

Of the 383 patients initially interviewed, 135 were excluded for the following reasons: 45 declined consent; 23 had been receiving hemodialysis treatment for less than three months and less than three sessions per week; 32 had rheumatologic disease; and 12 were elderly and suffering from age-related poor health and cooperation disorder. In addition 10 had mobilization/orthopedic problem including severe osteoarthritis (n=5), amputation (n=2), use of crutches (n=2) and confined to a wheelchair (n=1), seven had cerebrovascular disease sequelae, four were suffering from mental retardation, and two more hearing problems making participation unfeasible. As a result, 248 of the original 383 patients were included in the analysis. Of these, 36 (KDQOL-36) questionnaires were completed by all patients included in the study.
patients interviewed were included in the study. The demographic data for all 248 patients are shown in Table 1.

Table 1. Demographic characteristics of HD patients

| Characteristic                  | FMS group | Control group |
|--------------------------------|-----------|---------------|
| n (%)                          | 33 (13.3) | 215 (86.7)    |
| Age, mean ± SD                 | 65.06±8.92| 60.29±12.20** |
| Gender, men/women              | 0/33      | 115/100       |
| BMI                            | 27.05±5.14| 25.80±5.18*   |
| Hemodialysis duration (months), mean ± SD | 35.54±74.4| 69.38±63.20*  |
| Education level, no. (%)       | 9         | 71 (33) ***   |
| No schooling                   | 25 (75.79)| 8 (24.2)     |
| Primary school                 | 8 (24.2)  | 91 (42.33) ***|
| Junior or senior high school   | 0         | 41 (19.07) ***|
| College                        | 0         | 12 (5.6) ***  |
| WPI                            | 11.82±3.37| 0.71±1.38***  |
| SSS                            | 8.39±1.47 | 4.24±2.07***  |

FMS: Fibromyalgia Syndrome, SD: Standard Deviation, WPI: Widespread Pain Index, SSS: Symptom Severity Scale. *, p<0.05, **, p<0.01, ***: p<0.001

The major etiology of kidney failure was diabetes mellitus (32.7%) followed by hypertension (31.0%), although polycystic kidney disease (10.9%) was also responsible for a notable proportion of kidney failure. Additionally, various other causes accounted for 10.5% of kidney failure, while in 14.9% of the patients, the cause remained unknown. FM was identified in 33 (13.3%) patients and all of these patients with FM were female. The mean age was higher in the group with FM. In the FIQ evaluation of FM patients in CKD patients, the mean±standard deviation (range) FIQ score was 72.48±14.41 (31.33-89.67). The WPI and SS scores were higher in the FMS group, as expected (p<0.001). There was no statistically significant relationship between FM and BMI or dialysis duration in patients (p>0.05). However, the level of education was lower in the patients diagnosed with FM (p<0.05). Frequency of FM decreased as education level increased.

Table 2 shows the comparison of laboratory parameters of patients with and without FM. The difference between the laboratory parameter results of the groups was not statistically significant.

Table 2. The laboratory results of HD patients in the FM and control groups (Mean±SD)

| Parameter                        | FM Group (n=33) | Control Group (n=215) |
|----------------------------------|-----------------|----------------------|
| Hemoglobin, g/dL                 | 11.49±1.48      | 11.47±1.48*          |
| Albumin, g/dL                    | 3.93±0.55       | 3.98±0.41*           |
| Bun                              | 64.24±17.93     | 65.09±16.73*         |
| Creatinin                        | 7.28±1.46       | 7.96±2.45*           |
| CaXP (mg/dL)                     | 42.23±11.02     | 40.56±10.15*         |
| Kt/V                             | 1.59±0.23       | 1.50±0.33*           |
| Parathyroid hormone, pg/mL       | 418.88±582.88   | 345.86±355.42*       |
| Alkaline phosphatase, IU/L       | 156.75±174.43   | 123.90±84.41*        |

SD: Standard Deviation, CaXP: CalciumxPhosphorus, Kt/V= index of dialysis adequacy, FM: Fibromyalgia Syndrome. *, p<0.05

When compared to patients without FM, all parameters from the SF-36 quality of life and KDQOL-36 score scale sub-parameter results were found to be lower in the patients with FM diagnosis (p<0.05) (Table 3).

Discussion

Musculoskeletal system disorders are relatively common in patients with CKD. These disorders, having a wide spectrum which includes FM, are observed in about 60% of hemodialysis patients.9,10 However, there are some studies in the literature examining the frequency of FM in individuals with CKD.

FM frequency has been evaluated in hemodialysis patients and the results are contentious. A study conducted in Turkey by Yuceturk et al. reported the frequency of FM to be 7.4% in hemodialysis patients, whereas Couto et al. found the FM prevalence to be 3.9%.12,13 Samimagham et al. investigated a cohort of Iranian hemodialysis patients and reported an FM frequency of 12.2%.14 Leblebici et al. studying another Turkish cohort of 221 hemodialysis patients to be 9%.15 In the USA, Wolfe et al. investigating 3006 individuals from the general population found the FM prevalence to be 2%; 3.4% in females, and 0.5% in males.16 In the present cohort the FM frequency was 13.3%, higher than the normal population.

Although FM is observed in all ethnic groups, and across the age groups and genders, it is most prevalent in the female 40-60 age group.7 While previous studies12,14 of hemodialysis patients have reported a female preponderance, Leblebici et al. did not find any relationship between gender and FM in their study on hemodialysis patients.15 In our study, 100% of the 33 patients with a diagnosis of FM were women. FM was not observed in male patients, which is in contrast to the findings reported by Wolfe et al where 0.5% of cases of FM in the general population were identified in males.

FM frequency has been reported to increase with age, and the frequency of relapse decreases at more advanced ages.6,16 Nevertheless, in earlier studies of the prevalence of FM in hemodialysis patients, no statistically significant

Table 3. Comparison of SF-36 Quality of Life and KDQOL-36 Score Scale Sub-Parameter Results of HD patients in the FM and control groups (Mean±SD)

| Parameter                        | FM Group (n=33) | Control Group (n=215) |
|----------------------------------|-----------------|----------------------|
| Physical functioning             | 24.39±7.12      | 60.20±30.54**        |
| Role-physical                    | 0.00±0.00       | 17.60±37.02*         |
| Role-emotional                   | 29.29±15.12     | 55.50±43.59*         |
| Energy/fatigue                   | 25.30±18.19     | 47.76±20.20**        |
| Emotional well-being             | 57.93±20.69     | 68.72±18.27*         |
| Social functioning               | 36.74±29.80     | 69.53±32.57**        |
| Pain                             | 16.21±16.53     | 36.13±19.99**        |
| General health                   | 30.37±20.73     | 85.43±21.25**        |
| SF-12 PCS                        | 25.24±5.66      | 37.96±9.03**         |
| SF-12 MCS                        | 37.62±10.78     | 45.62±11.46**        |
| Burden of kidney disease         | 20.07±20.89     | 37.40±25.73**        |
| Symptoms/problem list            | 69.69±8.76      | 83.96±9.50**         |
| Effects of kidney disease        | 63.07±14.64     | 75.96±16.66**        |

SD: Standart Deviation. SF-36: Short Form-36, KDQOL-36: Kidney Disease Quality of Life-36, SF-12 PCS: Short Form-12 Physical component summary score, SF-12 MKS: Short Form-12 Mental component summary score, FM: Fibromyalgia Syndrome. *, p<0.05, **: p<0.01
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When the KDQOL-36 questionnaire was completed by our participants a decrease in all sub-parameter scores in hemodialysis patients with a diagnosis of FM was found when compared to hemodialysis patients without FM.

Conclusion
In the present study the FM prevalence in hemodialysis patients (13.3%) was higher than the general population and more frequent in female patients. No relationship was identified between laboratory parameters, BMI, hemodialysis duration, and Kt/V values of the patients and FM. However, FM was reported to negatively affect the QOL by hemodialysis patients. To counter this decrease in QOL, measurement of laboratory parameters is not sufficient, it we believe that is also important to evaluate FM, which is increased in frequency in these patients, particularly in women when compared to the general population. In conclusion, we believe that FM, which reduced both SF-36 and KDQOL-36 scores across all sub-parameters, should be an important element of diagnosis that should be investigated in hemodialysis patients routinely during follow up.

Conflict of Interest
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