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Pain-related Factors in Hemodialysis Patients

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Abstract

Background: Pain is a prevalent issue among patients undergoing hemodialysis (HD). This study aimed to evaluate the prevalence of pain and identify factors associated with pain in HD patients.

Methods: Two hundred two HD patients participated in the study. Demographic and clinical data, pain characteristics, and sleep quality were recorded. Symptom burden and pain severity were assessed using the Edmonton Symptom Assessment Scale (ESAS) and the McGill-Melzack Pain (MGP) questionnaire.

Results: The majority of participants were male (59.9%), with a mean age of 59.6±12.7 years. Pain was reported by 80.2% of the patients and was significantly more prevalent among females (p=0.001) and individuals with lower educational levels (p=0.005). Median ESAS and MGP scores were 20 (range: 4-84) and 47 (range: 22-84), respectively. Patients reporting pain had significantly higher levels of CRP (p=0.044), parathyroid hormone (p=0.005), and higher ESAS scores (p=0.001). Sleep quality was impaired in 37% of patients. ESAS scores were significantly higher among females (p=0.003), those with impaired sleep quality (p<0.001), and regular analgesic users (p=0.002). MGP scores were significantly elevated in patients with diabetes (p=0.002), lower educational attainment (p=0.022), daily pain occurrence (p<0.001), and poor sleep quality (p<0.001). Additionally, patients with pain in multiple body regions reported higher MGP scores (p<0.001). There was a significant correlation between MGP scores, age (p=0.001), and ESAS scores (p<0.001).

Conclusion: Pain is highly prevalent among HD patients and is associated with female gender, lower educational level, elevated CRP, and higher parathyroid hormone levels. The severity of pain is particularly influenced by diabetes, low education level, and the number of painful body regions. Moreover, pain significantly impacts symptom burden and sleep quality.

Keywords: Hemodialysis, Pain, Quality of Life, Sleep

INTRODUCTION

Hemodialysis (HD) patients commonly experience various symptoms affecting multiple organs and systems, with pain being among the most frequent complaints (1). Although reported pain prevalence varies depending on the assessment methods used, it remains notably high (2,3). Pain severity in HD patients ranges broadly from mild discomfort to severe pain.

Pain significantly contributes to sleep disturbances and psychosocial challenges in HD patients (4). Additionally, it is closely linked with depression, decreased quality of life, increased disease burden, and impaired sleep quality (5). If left untreated, pain can result in shortened or missed dialysis sessions, increased hospitalization rates, and frequent visits to healthcare facilities (6). Furthermore, persistent pain has a detrimental impact on patient survival (7). Therefore, systematic assessment, effective management, and identification of factors related to pain are essential components of comprehensive care in HD patients.

This study aimed to evaluate the prevalence, intensity,

and factors associated with pain among HD patients.

METHODS

Patients

We conducted this study by face-to-face questionnaire at the hemodialysis unit of the Ondokuz Mayıs University. Inclusion criteria were ≥age 18 years, HD duration ≥one year, and adequate cognitive function. Exclusion criteria were the presence of cancer and/or overt infection. A total of 202 patients gave informed consent for participation.

Socio-demographic information such as age, gender, and educational status of the patients were questioned. Duration and etiology of chronic kidney disease (CKD), HD vintage, comorbidities, dialysis vascular accesses (fistula or catheter), and the polymerase chain reaction (PCR) positive COVID-19 history of the patients were recorded. The presence of pain was questioned in all patients. In patients with pain, the duration and frequency of pain, its effect on daily life and sleep quality, the use of drug therapy for pain, and whether they used alternative medicine for pain were determined. Hemoglobin, albumin, C-reactive protein (CRP), parathormone (PTH), urea reduction rate (URR), fractional urea clearance (KT/V), and other biochemical parameters were obtained from the medical records. Pain and symptom burden were assessed using the McGill-Melzack Pain (MGP) and Edmonton Symptom Assessment System (ESAS) questionnaires. The presence of pain for more than 3 months is characterized as 'chronic'.

McGill-Melzack Pain (MGP) Questionnaire

The McGill-Melzack Pain (MGP) questionnaire is widely utilized internationally to assess pain. The questionnaire comprises four sections that evaluate pain location, characteristics, temporal changes, factors influencing pain intensity, and the overall severity. Pain severity is determined by descriptive terms such as mild, uncomfortable, annoying, distressing, terrible, and unbearable. Additionally, pain intensity is quantified through a numerical scoring system ranging from 0 to 112 points. This questionnaire has been previously applied in assessing pain among hemodialysis patients (8). The Turkish version's validity and reliability were confirmed by Oksuz et al. in 2007 (9).

Revised Edmonton Symptom Assessment System

The Edmonton Symptom Assessment System (ESAS) assesses pain, fatigue, drowsiness, well-being, nausea, appetite, shortness of breath, depression, anxiety, and itching. Each symptom is rated on a scale of 0-10 (minimum-maximum).

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS Statistics for Windows, version 15.0 (SPSS Inc., Chicago, IL, USA). Normality of data distribution was assessed with Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistics were presented as means, medians, numbers, and percentages. The independent samples t-test was used to analyze numerical variables with normal distribution, while the Mann-Whitney U test was applied for variables without normal distribution. Chi-square analysis was conducted for comparisons of categorical data. Spearman's correlation test was employed to evaluate correlations. Statistical significance was set at a p-value of less than 0.05.

RESULTS

Most participants (59.9%) were male (mean age 59.6±12.7 years). Median HD duration was 3 years (1-22). The most common CKD etiologies were hypertension (43.1%) and diabetes (32.7%), respectively. AV fistula was used in 72.3%, and tunneled catheters were used in 25.7% as vascular access. 26.2% of the patients had COVID-19 infection (**Table 1**).

Most of the patients (80.2%) had pain. Almost all (90.1%) had chronic pain (≥12 months in 71% of the patients). The frequency of pain was 'daily' in 34% of the patients and 'a few days in a week' in 35.2%. When the patients were asked how often the pain affects their daily life, 43.8% answered 'sometimes', 29% 'often', and 8.6% 'always'. In addition, 37% of the patients stated that pain affected their sleep quality (**Table 2**).

Most of the patients (91.4%) used medications for pain. Frequently used medications are; paracetamol (56.8%), pregabalin/gabapentin (25.9%), and NSAID (21%). About one-fifth of the patients (16.7%) used medication regularly, and 54.9% used it only when needed. 26.5% of the patients used antidepressants, and 12.3% applied alternative medicine methods for pain. Apart from dialysis physicians, internal medicine physicians (34.6%), a nephrologist (17.9%), orthopedics (13.6%), and algology specialists (12.3%) were consulted for pain, respectively. Patients frequently had their pain medication prescribed by dialysis physicians (78.4%). Additionally, 25.7% and 44.6% of the patients were admitted to family and other specialist physicians, respectively (**Table 2**).

Analysis of ESAS and MGP Questionnaires

The patients' median ESAS and MGP scores were 20 (4-84) and 47 (22-84), respectively. According to the MGP scale, patients classified their pains as follows; 18.5% 'mild', 45.1% 'discomforting', 27.2% 'distressing', 8% 'horrible', and 1.2% 'excruciating'. The lower extremity (61.1%) was the most common site of pain. This was followed by the upper extremity (35.8%) and the lower back (13%). 29.6% of patients reported pain in at least two body regions. Pain frequency was higher in women (p=0.001) and lower educated (p=0.005). In patients with pain, CRP (p=0.044) and PTH (p=0.005) levels were higher. In addition, ESAS (p=0.001) scores were higher, too. However, age, CKD duration, CKD cause, dialysis

Table 1. Demographic, laboratory, and pain-related characteristics of patients

Parameters	Mean +/-SD
Hemoglobin (g/dL)	11.0 ± 1.3
Albumin (g/dL)	3.5 ± 0.3
Parathormone (pg/mL)	369 (14-2982)
URR (%)	71.8 (38.7-88)
Kt/V	1.5 (0.6-2.5)
(Ca) x (P)	43.4 (16-100)
CKD etiology, n (%)	
Hypertension	87 (43.1)
Diabetes mellitus	66 (32.7)
PKD	16 (7.9)
Glomerulonephritis	12 (5.9)
Others	12 (5.9)
Unknown	9 (4.5)
Vascular access, n (%)	
AV fistula	146 (72.3)
Tunneled catheter	52 (25.7)
COVID-19 history (positive)	53 (26.2)
Presence of pain, n (%)	162 (80.2)
Pain duration	
<3 months	16 (9.9)
3-6 months	13 (8.0)
7-12 months	18 (11.1)
>1 year	115 (71.0)
Pain frequency, n (%)	
Daily	55 (34.0)
Few days a week	57 (35.2)
Few days in a month	27 (16.7)
Rarely	23 (14.2)
Impact on quality of life, n (%)	
Never	2 (1.2)
Rarely	28 (17.3)
Sometimes	71 (43.8)
Most of the time	47 (29.0)
Anytime	14 (8.6)
Poor sleep quality,n (%)	60 (37)

*URR; urea reduction ratio, Kt/V; fractional urea clearance, (Ca)x(P); calcium phosphorus product, CKD; chronic kidney disease, PKD; polycystic kidney disease, AV; arteriovenous.

duration, comorbidity, vascular pathway, COVID-19 history, hemoglobin, albumin, URR, KT/V, and (Ca) x(P) product did not differ between groups (Table 3).

Females' ESAS scores were significantly higher than males. The MGP score was higher in those with lower education. Those with diabetes and coronary artery disease (CAD) had a higher MGP score than those without (p=0.003). No significant difference in ESAS score was observed according to comorbidities. ESAS scores were higher for limb pain (p=0,002) and back pain (p=0,003) and lower for head pain (p=0,002). MGP scores were higher for upper extremity (p=0.023) and back (p=0.003) pain and lower for headache (p=0.030). Those with two or more painful sites had a higher MGP score than those with pain in one site (p<0.001) (Table 4). ESAS and MGP scores were significantly higher in those whose pain interfered with daily activities and sleep (p<0.001). ESAS and MGP scores differed significantly according to pain frequency (p<0.001). ESAS and MGP scores were significantly higher in those with daily pain than in the others (Table 4).

Table 2. Characteristics of patients regarding pain management

Analgesic use, n (%)		148 (91.4)
Analgesic type,n (%)		
Paracetamol		92 (56.8)
Pregabalin/gabapentin		42 (25.9)
NSAID		34 (21.0)
Herbal supplement		31 (19.1)
Topical analgesic		18 (11.1)
Opioids		10 (6.2)
Others		7 (4.3)
Frequency of analgesic use, n (%)		
Regularly		27 (16.7)
Sometimes		18 (11.1)
When needed		89 (54.9)
Rarely		28 (17.3)
Antidepressant use,n (%)		53 (26.5)
Complementary or alternative medicine, n (%)		20 (12.3)
Specialties admitted for pain palliation other than dialysis physician	Internal medicine	56 (34.6)
	Nephrology	29 (17.9)
	Orthopedics	22 (13.6)
	Algology	20 (12.3)
	Neurology	11 (6.8)
	Neurosurgery	5 (3.1)
	Others	19 (11.7)
Prescribing pain medication	Dialysis physician	116 (78.4)
	Family physician	38 (25.7)
	Other physicians	66 (44.6)

Herbal supplement users had significantly higher MGP scores than others (p=0.045). ESAS and MGP scores were significantly different between groups according to frequency of analgesic use. The ESAS and MGP scores of patients who used analgesics regularly were higher than the others (p<0.05). The ESAS scores of patients who were prescribed analgesics by specialists were significantly lower than those who were not prescribed analgesics by specialists (p=0.043) (Table 5).

In the correlation analysis, the ESAS score was moderately correlated with the MGP score (r: 0.412; p<0.001). MGP score was weakly associated with age (r: 0.214; p=0.001).

DISCUSSION

Chronic kidney disease is a global problem with increasing prevalence, and patients' life is negatively impacted by the complications of CKD. Pain is a factor that has an impact on patients' quality of life and sleep. Most patients in our study had chronic and severe pain. Over 50% of HD patients experience pain (2,3). In this study, most of our HD patients (80.2%) experienced pain. On the other hand, about half of our patients had a level of pain that was severe or more severe. Pain severity affects quality of life, as is well known. Pain severity tends to be high in HD patients (2,3,10). The study by Er and colleagues showed that pain was intolerable in 6.7%, very severe in 10% and severe in

Table 3. Comparison of the patients according to the presence of pain

Factors	Pain (+) (n=162)	Pain (-) (n=40)	p-value
Age (years)	60.1 ± 12.6	57.7 ± 13.1	0.295
Gender (Female) (%)	74 (45.7)	7 (17.5)	0.001
Education level (Low)	104 (64.2)	16 (40)	0.005
CKD duration (years)	5 (1-40)	5 (1-23)	0.716
CKD etiology,n (%) • Hypertension • Diabetes	 68 (42) 57 (35.2)	 19 (47.5) 9 (22.5)	 0.527 0.126
Hemodialysis vintage	3.5 (1-22)	3 (1-20)	0.827
COVID-19 history	44 (27.2)	9 (22.5)	0.548
Hemoglobin (g/dl)	11.0 ± 1.3	10.8 ± 1.5	0.388
Albumin (g/dl)	3.5 ± 0.3	3.5 ± 0.2	0.516
CRP (mg/L)	9 (0.1-164)	4.6 (1-148)	0.044
PTH (pg/mL)	400 (14-2982)	279 (52-1324)	0.005
URR (%)	71.8 (38.7-88)	71.3 (48.6-85)	0.604
Kt/V	1.5 ± 0.3	1.5 ± 0.3	0.952
(Ca) x (P)	42.8 (16-100)	44.9 (20-98.4)	0.357
ESAS	21 (4-84)	13 (5-53)	0.001

CKD; chronic kidney disease, CRP; C-reactive protein, PTH; parathormone, URR; urea reduction ratio, Kt/V; fractional urea clearance, (Ca) x (P); calcium phosphorus product, ESAS; Edmonton Symptom Assessment Scale

31.7% of their patients (11). The frequency of pain is also a crucial issue. Er et al. also stated that 53.7% of their patients experienced pain at least once a week (11). Furthermore, almost all our patients had chronic pain, and a significant proportion (71%) had pain for over a year. Similarly, Gamondi et al. showed that the majority of HD patients (84%) experienced chronic pain (3).

It is a widespread pain that concerns the whole body in dialysis patients. Extremity pain was the most common in our patients. Similarly, Fleishman et al. show that foot pain was the most common site of pain in dialysis patients (62.5%) (12). Bone mineral disorders, osteoarthritis, and comorbid diseases such as diabetes could be responsible for this. In this study, patients with ≥ 1 painful region also had higher MGP scores. Similarly, severe pain was associated with ≥4 painful regions in the study by Fleishman et al. (12).

Approximately one-third of the patients stated that the pain affected their sleep. Also, pain severity is higher in those whose sleep quality is affected. Sleep quality is poorly affected in HD patients (11,13). Poor sleep quality is associated with depression (14). Similarly, increased pain severity causes sleep problems in HD patients, as shown by Harrison et al (15).

Pain frequency was higher in women. Samoudi and colleagues have shown that pain has a major effect on the quality of life of HD patients. Older patients, women and the uneducated are at high risk (16). In the study by Gamondi et al, similar to our findings, the female gender was the determining factor for the presence and intensity of pain in HD patients (3). There is a gender difference in pain sensitivity. Women report more considerable pains in more body areas than men. Some painful diseases are more common in women, and for many conditions, symptoms differ between women and men. Genetic, physiological, neuronal, hormonal, psychological, and social factors can mediate the difference in pain between men and women (17). Changes in estrogen plasma levels have been associated with recurrent pain in women (18). In addition, women seeking medical help more than men may cause a higher incidence of pain in women (17). Educational levels were lower among patients with pain in our study. Fleishman et al. reported a relationship between education level, income level, and pain in HD

Table 4. Comparison of patient and pain-related factors in terms of ESAS and MGP scores

Factors		ESAS Median (min-max)	P value	MGP Median (min-max)	P value
Gender	Female/Male	23(4-62)/17(4-84)	0.003	48.5 (22-84)/46(22-84)	0.302
Education level	Low/High	21 (4-84)/16.5(4-61)	0.057	52(22-84)/44(26-71)	0.022
Comorbidity	Diabetes(+)/(-)	20.5(4-84)/18.5(4-62)	0.210	52(24-84)/44 22-72)	0.003
	CAD(+)/(-)	21.5(4-84)/18.5(4-67)	0.291	53(22-84)/45.5(24-78)	0.003
COVID-19 history	(+)/(-)	16(4-50)/20(4-84)	0.236	53(26-77)/46(22-84)	0.316†
Pain frequency	Daily Few days a week Few days in a month Rarely	28 (11-84) 19 (4-61) 15 (7-51) 16 (4-45)	<0.001	55 (26-84) 51 (24-75) 45 (22-62) 41 (27-66)	<0.001
Pain impact on quality of life	Low/ High	17(4-52)/28(6-84)	<0.001	43(22-72)/56 (32-84)	<0.001
Impact on sleep quality	Yes/No	29 (4-84)/18(4-51)	<0.001	54.5(24-84)/ 44.5(22-75)	<0.001
Body pain region	Low extremity (+)/(-)	25(4-67)/16(4-84)	0.002	51(24-78)/45(22-84)	0.051
	Upper extremity (+)/(-)	21.5(4-67)/20.5(4-84)	0.987	54(27-78)/46(22-84)	0.023
	Head (+)/(-)	14(4-30)/22(4-84)	0.002	42(26-68)/49(22-84)	0.030
	Back (+)/(-)	28(13-67)/20(4-84)	0.00	60(37-75)/46(22-84)	0.003
The number of the painful region	One/Two or More	20(4-84)/25(4-67)	0.251	45(22-84)/57(34-78)	<0.001

ESAS; Edmonton Symptom Assessment Scale, MGP; McGill-Melzack Pain, CAD; coronary artery disease

Table 5. Comparison of patients' ESAS and MGP scores according to pain management-related characteristics

Factors		ESAS Median (min-max)	P value	MGP Median (min-max)	P value
Complementary or alternative medicine use	Yes/No	20 (4-43)/ 21.5 (4-84)	0.226	45 (32-78)/ 48 (22-84)	0.799
Analgesic use	Paracetamol (+)/(-)	20 (6-84)/ 22 (4-67)	0.997	48.5 (22-84)/ 46 (27-75)	0.855
	Pregabalin/gabapentin (+)/(-)	21.5 (4-67)/ 20.5 (4-84)	0.957	50 (26-78)/ 46 (22-84)	0.254
	NSAID (+)/(-)	21 (4-67)/ 20.5 (4-84)	0.608	45.5 (26-71)/ 48 (22-84)	0.386
	Herbal product (+)/(-)	19 (4-64)/ 21 (4-84)	0.198	42 (30-65)/ 51 (22-84)	0.045
Frequency of analgesic use	Regularly Sometimes When needed Rarely	35 (10-53) 19.5 (8-46) 19 (4-84) 21.5 (4-51)	0.002	62 (36-77) 44.5 (26-64) 46 (24-84) 42.5 (22-75)	<0.001
Antidepressant use	Yes/No	22 (4-61)/ 18 (4-84)	0.173	51 (26-77)/ 46 (22-84)	0.143
Physician prescribing analgesic	Dialysis physician (+)/(-)	20 (4-84)/ 22 (4-62)	0.495	48.5 (22-84)/ 46.5 (30-78)	0.742
	Other physicians (+)/(-)	17 (4-61)/ 22 (4-84)	0.043	47 (22-71)/ 51 (24-84)	0.640
	Family physician (+)/(-)	19.5 (4-62)/ 200.5 (4-84)	0.638	51 (22-78)/ 48 (26-84)	0.719

ESAS; Edmonton Symptom Assessment Scale, MGP; McGill-Melzack Pain, CAD; coronary artery disease

patients (12). The low level of education may make it difficult for patients to understand the causes of pain. In addition, these patients may have problems reaching the right resources for pain and using them appropriately.

CRP and PTH levels were higher in patients with pain. Inflammation can cause pain, and CRP levels are increased in various diseases that cause chronic pain (19-21). Secondary hyperparathyroidism can cause significant bone pain (22). A study showed that high PTH levels were a determinant of chronic pain (23). A positive relationship between pain and PTH levels in HD patients has been shown in another study (24). Similar to our study, Ghonemy and colleagues found a relationship between pain and elevated CRP and PTH levels. The authors have suggested that CRP is a sensitive marker for increased perception of pain (25).

Patients with pain are expected to have a high ESAS score. In our study, the ESAS score was elevated in patients with a high frequency of pain, those who stated that pain affected daily life and sleep quality. Since this scale assesses the burden of patients' symptoms such as fatigue, pain, nausea, anorexia, anxiety and depression together, scores may be higher in women. The frequency of depression and anxiety increases in kidney failure patients, associated with poor prognoses such as hospitalization and mortality (26). There is a bidirectional relationship between pain and depression. The patient's emotional state may change by pain. Depression also aggravates pain symptoms (27). In our study, MGP scores correlated with age. Although pain threshold and sensitivity change with age, the frequency of chronic pain increases with age. The prevalence of chronic pain in the general population over 65 is approximately 40% (28).

Pain symptoms such as joint pain, chest pain, headache and muscle pain are very common in people recovering from COVID-19 (29). Therefore, a higher frequency of pain can be expected in patients with COVID-19. However, our study did not detect any effect of COVID-19 status on patients' pain frequency, ESAS, and MGP scores. Since the frequency of chronic pain and the rate of analgesic use are high in our patients, evaluating the effect of COVID may require a more detailed examination. However, our study was not designed for this purpose.

Most of the patients in our study received pharmacological treatment for pain management. One in five used non-pharmacological treatment for pain. Paracetamol is the first choice of non-opioid drug in HD patients. NSAIDs can decrease residual renal function and cause gastrointestinal bleeding, uncontrolled hypertension, and hyperkalemia, but they can be used by closely monitoring the side effects (30). These concerns can explain the lower rates of NSAID use in our study. In the study of Fleishman et al., 66.1% of the patients used pharmacological pain treatment (12). However, analgesic treatment rates in patients were not expressed. In addition, in the same study, 24.5% of the patients used non-drug treatments for pain. Very few opioids have been prescribed to our patients. The prescribing policy in our country and the fear of the side effects may be responsible for this situation.

Non-dialysis CKD patients frequently prefer herbal products, but these treatments may increase the risk of kidney failure (31). On the other hand, there may be interactions between pharmacological agents and herbal supplements. Bhall et al. stated that kidney failure patients must inform their physicians before using herbal products, posing a significant health risk (32). By evaluating the pain characteristics and causes, as well as the treatments for pain palliation, patients can be prevented from being exposed to the side effects of these products.

In our study, we found that the majority of patients presented with pain complaints to physicians other than the dialysis physician and the nephrologist.

There are two important reasons for admitting to other specialties. First, as in previous studies, pain palliation cannot be adequately achieved in most dialysis patients, and patients seek different treatments (2). Secondly, because the causes of pain differ, patients apply to other specialties. These reveal the importance of a multidisciplinary approach to pain management.

Limitations of the Study

There are a number of limitations to our study. Our study was single-center and the number of patients was limited. Multicentric studies involving more patients will help overcome limitations in understanding and addressing pain-related problems. This survey study may not be sufficient to explain some cause-and-effect relationships. In addition, the pain etiology of the patients was not evaluated (neuropathic, ischemic, degenerative, etc.). Although the effect of pain on sleep and daily life has been questioned, clinical conditions that have been shown to affect pain, such as depression and anxiety levels, have not been studied. However, evaluating pain-related factors and symptom burdens in a large patient group makes our study powerful. On the other hand, in our study, the evaluation of both pain and pain-related quality of life markers and symptom burden with 2 different scales provided a more objective evaluation in patients.

CONCLUSION

Our findings underscore that pain is a prevalent and significant problem among HD patients. Regular assessment and monitoring of pain can enhance the quality of life for these individuals. Increased awareness and early detection of pain may facilitate timely interventions, ultimately improving patient outcomes and their overall dialysis experience.

DECLARATIONS

Ethics committee approval: Ondokuz Mayıs University Clinical Research Ethics Committee approved the study (OMU KAEK: 2021/412). The study was conducted in accordance with the principles of the Declaration of Helsinki for research involving human subjects.

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