

Pain Assessment and Affecting Factors in Hemodialysis Patients

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Cite this article as: Ergül EE, Ergül Ç, Arslan YK. Pain assessment and affecting factors in hemodialysis patients. *Arch Basic Clin Res.* 2024;6(2):135-139.

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ABSTRACT

Objective: As a result of long-term damage to the nerves caused by harmful molecules in chronic renal failure patients who are treated with hemodialysis, the clinical manifestation defined as uremic neuropathy may occur in patients. In our study, we aimed to determine the prevalence of neuropathic pain in hemodialysis patients and to evaluate risk factors.

Methods: Patients over the age of 18 who underwent hemodialysis treatment were included in our study. Demographic characteristics of the patients, duration of dialysis, and comorbidities were recorded. The Brief Pain Inventory was used to assess the patients' pain intensity. The Neuropathic Pain Questionnaire and Neuropathic Pain Questionnaire; Short Form was employed for the evaluation of neuropathic pain.

Results: Neuropathic pain was detected in 25 (41.7%) of 60 hemodialysis patients. Chronic pain was evaluated with a Likert scale as 0: no pain 10: the worst pain I can imagine. The averages for the past week were categorized as pain worst, pain least, pain average, and pain now, and recorded as 5.9, 6.5, 6.4, and 6.4, respectively. The number of comorbid disorders and the scores of neuropathic pain questionnaire in short form were determined to be statistically associated ($P=.040$).

Conclusion: Neuropathic pain in hemodialysis patients was detected in 41.7% of the patients; it is a common symptom and is associated with the number of comorbid diseases. This study is an exemplary study in terms of evaluating the prevalence of neuropathic pain in hemodialysis patients. It has been a guide to start supportive treatments at an earlier period.

Keywords: Chronic pain, hemodialysis, neuropathic pain

INTRODUCTION

Neurological disorders are quite common in people undergoing hemodialysis treatment. They may be of central or peripheral origin, or they may be accompanied by disorders such as muscle damage and autonomic dysfunction.¹ When kidney disease impairs glomerular filtration, an accumulation of organic wastes develops, producing uremic neuropathy. In patients with end-stage renal disease, a decrease in glomerular filtration rate is observed. Uremic neuropathy most commonly involves the lower extremity in a distal symmetrical manner, and axonal disruption and local myelin injuries are seen in the pathogenesis. Uremic sensorimotor axonal neuropathy is a progressive and known complication in patients with end-stage renal

disease and on dialysis. However, the presence of definite polyneuropathy in dialysis patients needs to be investigated further, especially in our country.²

Uremic neuropathy can present with a variety of symptoms, but the primary manifestation is slowly progressive sensorimotor axonal polyneuropathy that starts in the distal lower extremities and eventually spreads up to the proximal, occasionally involving the upper extremity.^{3,4} Early symptoms include paresthesia, feelings of warmth and cold, increased pain, cramps and restless legs syndrome. In the long term, symptoms such as loss of strength in the lower extremities, changes in deep tendon reflexes, muscle atrophy, loss of balance, and numbness can be seen.⁵

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Received: June 16, 2023

Revision requested: October 16, 2023

Last revision received: November 20, 2023

Accepted: December 25, 2023

Publication Date: May 27, 2024

There have been numerous studies examining the association between peripheral neuropathy and end-stage renal disease. In studies conducted in developed countries, more than 60% of findings of uremia or diabetes-induced polyneuropathy were found in patients with end-stage renal disease. In most of them, subclinical disease was observed when evaluated by nerve conduction studies.¹

Neuropathic pain is a symptom that is more common in patients undergoing hemodialysis treatment and affects quality of life. The main objective of our study was to examine the incidence of neuropathic pain and factors in hemodialysis patients. The main purpose of our work is to investigate the prevalence of neuropathic pain and factors in patients receiving hemodialysis treatment. It is important to detect the presence of neuropathic pain in patients with chronic kidney disease (CKD) and to follow up on the neuropathic pain in addition to the treatment of CKD in order to increase the quality of life of the patients.

It can be predicted that neuropathic pain and polyneuropathy can be prevented by the early initiation of dialysis treatment and renal transplantation in patients with CKD.

MATERIAL AND METHODS

A total of 19 women and 41 men (age range: 27-96 years) who were treated with hemodialysis for end-stage renal disease were included in the study. The hemoglobin, blood potassium, sodium, calcium, phosphorus, magnesium, B12, and folic acid levels, which are predicted to affect neuropathy findings, were evaluated before the study, and patients with laboratory findings different from normal were excluded from the study. The patients were categorized into 3 groups as <2 years, 2-7 years, and >7 years according to the duration of dialysis. As additional diseases, hypertension, diabetes, stroke, cardiovascular

diseases, chest diseases, and neurological diseases were questioned. Patients with diabetes, one of these conditions that may potentially be the source of neuropathic pain, were not allowed to participate in the research. Patients were questioned about medication use for neuropathic pain before and during dialysis. Patients using gabapentin, pregabalin, and patients using alpha lipoic acid used in diabetic polyneuropathy were not included in the study.

Pain assessment of the participants was made with the Brief Pain Inventory. The Neuropathic Pain Questionnaire and the Neuropathic Pain Questionnaire Short Form which Turkish validity and reliability studies were carried out in the evaluation of neuropathic pain, were used. The neuropathic pain rates of the patients were determined, and their association with age, gender, dialysis duration, comorbidities, and sociodemographic data were evaluated.

Written informed consent was obtained from all patients included in the study. Erzincan Binali Yıldırım University Clinical Research Ethics Committee approved this study in a decision dated January 19, 2023 and meeting number: 02, decision number: 2023-02/3. The Declaration of Helsinki's guiding principles were followed in conducting the study.

Statistical analysis was performed using International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS®) 22 (IBM SPSS Corp.; Armonk, NY, USA). Results were presented as numbers and percentages for categorical variables, mean \pm SD, median, and minimum–maximum for continuous variables. Chi-square or Fisher exact test was used to compare categorical variables between groups. The normality of the distribution for continuous variables was confirmed by the Kolmogorov–Smirnov test. In the comparison of independent continuous variables between the 2 groups, Student's *t*-test or Mann–Whitney *U*-test was used depending on whether the statistical hypotheses were met. The statistical significance level for all tests was accepted as $P < .05$.

RESULTS

The mean age of hemodialysis patients participating in our study was 59.2 ± 13.7 years. Nineteen females (31.7%) and 41 males (68.3%) dialysis patients were included. Fifteen people (25%) with dialysis duration <2 years, 29 people (48.3%) with 2-7 years, and 16 people (26.7%) with >7 years were included in our study. The median duration of dialysis was found to be 4.0 (range: 1-22). According to the number of comorbid diseases, 26.7% had no disease, 30% had 1 comorbid disease, 20%

MAIN POINTS

- Neuropathic pain is a symptom that is more common in patients undergoing hemodialysis treatment and affects quality of life. In this study, the rate of neuropathic pain was found to be 41.7% in hemodialysis patients.
- Uremic neuropathy can present with a variety of symptoms, but the primary manifestation is slowly progressive sensorimotor axonal polyneuropathy that starts in the distal lower extremities.
- As the number of comorbid diseases increases in hemodialysis patients, the presence of neuropathic pain increases, and it was statistically significant when evaluated according to the results of the short neuropathic pain questionnaire.
- Neuropathic pain in hemodialysis patients was determined independently of hemodialysis duration and age.

Table 1. Pain Assessment

	Mean \pm SD	Median	Minimum	Maximum
Pain worst	5.9 \pm 2.2	6.0	1.0	9.0
Pain least	6.5 \pm 2.1	6.0	3.0	10.0
Pain average	6.4 \pm 2.0	6.0	3.0	10.0
Pain now	6.4 \pm 2.0	6.0	2.0	10.0

had 2 comorbid diseases, 8.3% had 3 comorbid diseases, and 15% with 4% or more comorbid diseases.

Pain assessment of hemodialysis patients was determined with the Brief Pain Inventory: pain worst experienced in the last week, pain least experienced in the last week, pain average experienced in the last week, and pain now. It was recorded as "0: no pain, 10: worst pain imaginable" (Table 1). Similarly, the level of pain's effect on various activities was evaluated with a Likert scale as "0: It did not affect at all, 10: It completely prevented," and the results are summarized in Table 2. The level of affecting general activity, emotional state, walking, and normal work was above 6, and they were highly affected by the pain status of the patients. On the other hand, it had less effect on human relations, sleep, and enjoyment of life.

The average age of those with and without neuropathic pain was found to be similar in both the short and long neuropathic pain questionnaires (*P* values: .436; .440, respectively). The percentage of neuropathic pain in hemodialysis patients was found to be 41.7% in total in the province of Erzincan. According to the long neuropathic pain questionnaire, those with neuropathic pain were found to be 57.9% in women and 34.1% in men. Although the percentage of neuropathic pain in women is numerically higher, no statistically significant difference was found between men and women (*P* = .083). Similarly, although the percentage of neuropathic pain was higher in women in the short neuropathic

Table 2. Association Between Pain and Activity

	Mean \pm SD	Median	Minimum	Maximum
General activity	6.9 \pm 2.1	7.5	2.0	10.0
Emotion status	6.2 \pm 2.3	6.0	2.0	10.0
Walking	6.3 \pm 2.6	6.0	0	10.0
Normal work	6.2 \pm 2.6	6.0	1.0	10.0
Human relationship	3.4 \pm 2.8	3.0	0	9.0
Sleep	4.0 \pm 3.4	4.0	0	10.0
Enjoy life	4.3 \pm 3.1	5.0	0	10.0

pain questionnaire, it was not statistically significant (*P* = .121).

There was no difference in hemodialysis duration between those with neuropathic pain and those without neuropathic pain, and the results were similar for both short and long neuropathic pain questionnaires (*p* values: 0.764; 0.668, respectively). Similarly, there is no association between hemodialysis duration and activity (*p* values: 0.726). As the number of comorbid diseases increases in hemodialysis patients, the presence of neuropathic pain increases, and it was statistically significant when evaluated according to the results of the short neuropathic pain questionnaire (*P* = .040). However, the association between long neuropathic pain questionnaire results and comorbid disease was not statistically significant (*P* = .092).

DISCUSSION

Acute and chronic pain are very common complaints in hemodialysis patients. The presence of neuropathic pain in hemodialysis patients has been demonstrated in past studies.⁶ Many factors such as heredity, uremic and metabolic factors, various toxin accumulations, and low intake in the diet play a role in the pathogenesis of neuropathy in hemodialysis patients.⁷ In the determination of neurotoxins that cause uremic neuropathy, their concentration in plasma and the level of suppression of motor conduction velocity are taken into account.⁸ Nowadays, many extra treatments such as the use of highly dialyzable membranes, vitamin B, vitamin D, erythropoietin, and biotin supplements are used in hemodialysis patients. Although all these partially slowed down the progression of CKD, they were not effective in reducing the prevalence of neuropathy to the desired level.⁹

Our study aimed to investigate the prevalence of neuropathic pain and factors affecting neuropathic pain in patients receiving hemodialysis treatment in Erzincan province. It also aimed to determine how much it affects general activities, sleep, emotional status, walking, normal work, and the psychological state of the patients by evaluating pain in this patient group. The median value of the pain worst, pain least, pain average, and pain now in the last 1 week using the Brief Pain Inventory was found to be between 5.9 and 6.4, which strikingly shows the state of the pain felt in hemodialysis patients.

The experience of hemodialysis affects the quality of life in various countries and may be painful. Although pain is a prevalent symptom of CKD, the impact of pain on analysis and daily living activities has not been thoroughly explored in previous studies.¹⁰⁻¹² In this study, the effect of pain on general activity, emotional state, walking, and

normal working was significant, and its effect on human relations, sleeping and enjoying life was relatively less. In a previous study, similar to our study, in addition to the high prevalence of severe pain during hemodialysis, it was determined that pain had a high functional interaction, especially with general activity, disposition, and mobility.¹²

Approximately 60-100% of patients who are hospitalized to undergo dialysis treatment for CKD are affected by peripheral NP.² Bakre et al. found the clinical peripheral neuropathy rate to be 50% in patients followed up with CKD. When evaluated electrophysiologically, neuropathy was detected in 65% of the patients.⁸ In our study, the rate of neuropathic pain was found to be 41.7% in hemodialysis patients. The fact that neuropathy rates are relatively lower compared to other studies may be due to clinical evaluation only without electrophysiological study. In the case of electrophysiological examinations in asymptomatic hemodialysis patients, these rates may increase.

In the study by Bakre et al.,⁸ it was determined that males had a higher prevalence of neuropathy, even if this was not statistically significant. Contrary to this study, in our study, although it was not statistically significant, neuropathic pain was more common in women. On the other hand, a recent systematic review revealed a negative correlation between the proportion of female subjects and the prevalence of neuropathic pain in univariate regression analyses.¹³ The underlying reason for the conflicting results may be related to the distribution of the patient population and the number of individuals. Therefore, comprehensive studies in larger patient groups are needed.

Neuropathic pain caused by a disorder in the somatosensory system is more common in elderly patients with comorbid diseases.¹⁴ Three out of ten individuals who are older people (over the age of 70) report having neuropathic pain.¹⁵ Although neuropathic pain is more common, especially in a certain age group, no significant association was found between age and neuropathic pain in our study. Neuropathic complaints can also be detected in young people, especially in hemodialysis patients.

The results of the studies researching the association between the duration of hemodialysis and neuropathy are quite contradictory. In a group of fifty hemodialysis patients conducted by Al-Shazly et al.¹⁶ at Al-Azhar University, a relation was found between the duration of hemodialysis and neuropathy. In our study, on the contrary, neuropathic pain complaints were found to be independent of the hemodialysis duration of the patients. This discrepancy may be caused by overlap with comorbid diseases such as diabetes mellitus, which cause neuropathic pain in young patients.

Hypertension, diabetes, stroke, cardiovascular disease, chest disease, and neurological diseases were questioned as comorbid diseases in the study group. The increase in the number of comorbid diseases of the patients affects the formation of neuropathic pain. In our study, this effect was statistically significantly determined, especially in the results of the short neuropathic pain questionnaire.

The development of neuropathic pain may be influenced by numerous comorbid diseases. Neuropathic pain causes are metabolic (B12 deficiency, diabetic polyneuropathy), mechanical (carpal tunnel syndrome, radiculopathy, post-operative pain, phantom limb pain, cancer pain), inflammatory (postherpetic neuralgia, leprosy, HIV, Guillain-Barre syndrome, critical illness neuropathy), radiation, toxic (chemotherapy-induced, alcohol), and hereditary (Fabry disease, Charcot-Marie-Tooth disease).¹⁷ Neuropathy is seen in 20-50% of patients followed up with a diagnosis of diabetes.¹⁸ Considering all these, in our study, the number of comorbid diseases, including diabetes and neuropathic pain, was evaluated, and a significant association was found between them. In other words, the increase in the number of comorbid diseases in dialysis patients affects the presence of neuropathic pain. Although the number of publications examining comorbid diseases one by one is high, studies examining the total number of comorbid diseases like this study are very few in our country. Considering these results, it is necessary to evaluate hemodialysis patients not alone but together with all their comorbid conditions and arrange examination and treatment accordingly. In this regard, the study is quite instructive.

The most important inadequacy of this study is the lack of electrophysiological studies. Furthermore, making comorbid diseases a little wider and covering more diseases may provide more guiding information. In the future, there is a need for publications with larger patient populations and electrophysiological studies.

Ethics Committee Approval: The study was approved by the Erzincan Binali Yıldırım University Clinical Research Ethics Committee (date: January 19, 2023; meeting number: 02; decision number: 2023-02/3).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.E.E.; Design – E.E.E., Ç.E.; Supervision – E.E.E., Ç.E.; Resources – E.E.E.; Materials – E.E.E., Ç.E.; Data Collection and/or Processing – E.E.E., Y.K.A.; Analysis and/or Interpretation – E.E.E., Y.K.A.; Literature Search – E.E.E.;

Writing Manuscript – E.E.E.; Critical Review – E.E.E., Y.K.A.; Other – E.E.E., Ç.E., Y.K.A.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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