OVERVIEW OF PERIPHERAL NEUROPATHY IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING HEMODIALYSIS AT DR. MOHAMMAD HOESIN HOSPITAL PALEMBANG

Theresia Christin[1], Zulkhair Ali[2], Legiran[3], Ferawaty[4*]
[1]Staff of the Department of Neurology, Faculty of Medicine, Universitas Sriwijaya, Dr. Mohammad Hoesin Regional General Hospital, Palembang
[2]Staff of the Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya, Dr. Mohammad Hoesin Regional General Hospital, Palembang
[3]Staff of Anatomical Pathology Department of Medicine, Universitas Sriwijaya
[4]Resident of the Department of Neurology, Faculty of Medicine, Universitas Sriwijaya, Dr. Mohammad Hoesin Regional General Hospital, Palembang
E-mail: [1)] ferawaty05@yahoo.com

Abstract

Neurological complications occur in almost 60% of patients with advanced CKD and affect the nervous system at all levels, both central and peripheral. Peripheral neuropathy in CKD is usually asymptomatic until renal function is below 15%, and glomerular filtration is less than 10-12 ml/min. This study seeks to identify and characterize peripheral neuropathy in patients with chronic kidney disease undergoing hemodialysis at Dr. Mohammad Hoesin Hospital Palembang. This is a descriptive cross-sectional study with the research sample comprising chronic kidney disease patients undergoing hemodialysis at Dr. Mohommad Hoesin Palembang Hospital. The distribution of research subjects based on the Neuropathy Symptom Score (NSS) revealed that 65.7% fell into the mild neuropathy category, based on an NSS of 3-4. According to the electrophysiology results, 82.9% of patients exhibited peripheral neuropathy, while 17.1% showed normal NCS results. Sensory motor neuropathy accounted for 51.4%, including 71.5% with axonal neuropathy, 11.4% with axonal-demyelinating lesions, and no demyelinating lesions. The high prevalence of peripheral neuropathy in CKD patients identified through electrophysiological examination (ENMG) emphasizes the importance of nerve conduction examination as a diagnostic tool for peripheral neuropathy in CKD patients. This can aid in determining the progression of peripheral neuropathy in CKD patients, allowing for appropriate management and prevention of disability complications to enhance the quality of life for these individuals.

Keywords: *Chronic Kidney Disease (CKD), Neurological Complications, Peripheral Neuropathy, Hemodialysis, Glomerular Filtration Rate (GFR)*

1. INTRODUCTION

Chronic kidney disease (CKD) is a condition characterized by a glomerular filtration rate (GFR) below 60 mL/min/1.73m², albuminuria of at least 30 mg per 24 hours, or markers of kidney damage persisting for more than three months (Levin et al., 2013). The incidence of CKD varies globally, and it is believed to be higher than reported due to many cases going undetected. In the UK, the reported incidence is 10% of the population, rising to 15% in developing countries and peaking at 40% in individuals over 65 years of age (Ahmed et al., 2020). The etiology of CKD can stem from primary renal impairment or arise as a complication of multisystem disorders associated with comorbidities. Regardless of the cause, neurological complications are highly prevalent

in CKD, affecting nearly 60% of patients with advanced CKD and impacting the nervous system at all levels, both central and peripheral (Krishnan & Kiernan, 2009; Ramírez & Gómez, 2011). One notable neurological complication in the peripheral nervous system is peripheral neuropathy (Krishnan & Kiernan, 2009).

Peripheral neuropathy in CKD, commonly referred to as uremic neuropathy, stands as the most prevalent neurological complication associated with CKD. The suspicion of uremic neuropathy dates back to Charcot (1880) and Osler (1892). Since the advent of hemodialysis and kidney transplantation in the early 1960s, uremic neuropathy has undergone comprehensive study. Uraemia is recognized as the second leading cause of frequent metabolic neuropathies (Ramírez & Gómez, 2011). Patients typically manifest symptoms such as loss of sensation, pain, and weakness. In the early stages of uremic neuropathy, signs and symptoms include a reduction in sensory function in the distal parts during nerve conduction studies, diminished sensitivity to vibration, and the potential disappearance of tendon reflexes in the lower limbs (Krishnan & Kiernan, 2009; Ramírez & Gómez, 2011). Peripheral neuropathy in CKD generally evolves over months, although it can progress rapidly, resulting in significant disability (Ramírez & Gómez, 2011).

According to the article review, symptoms of neuropathy are reported in 60 to 100% of patients undergoing dialysis (Krishnan & Kiernan, 2009; Ramírez & Gómez, 2011). In a study by Gondhali et al. (2020), the prevalence of neuropathy in prehemodialysis and hemodialysis CKD patients was 55% and 80%, respectively (Gondhali et al., 2019). Another study conducted in India found that the prevalence of peripheral neuropathy disorders in the hemodialysis group was as high as 98% (Perkins & Bril, 2014). Peripheral neuropathy in CKD is typically asymptomatic until kidney function drops below 15%, with glomerular filtration less than 10-12 ml/min (Fatima et al., 2021). Several previous studies indicate that the prevalence of peripheral neuropathy in CKD patients, as determined by nerve conduction studies (NCS) examination, is significantly higher compared to patient-reported complaints and symptoms. For instance, in a study by D. Jasti et al. (2017), the prevalence of peripheral neuropathy in CKD patients was found to be 89% based on electrophysiological examination (NCS). This aligns with the findings of M. Al-Shazly et al. (2020), who reported 76% of polyneuropathy cases based on NCS results.

The high prevalence of peripheral neuropathy in CKD patients, as identified through electrophysiological examination (ENMG), underscores the utility of nerve conduction examination as a diagnostic tool for peripheral neuropathy in CKD patients (Fatima et al., 2021). Nerve conduction examination (NCS) stands as the gold standard method for diagnosing neuropathy and determining the specific type of peripheral neuropathy. Widely adopted for its accuracy, reliability, and objectivity, NCS enables the assessment of the extent of peripheral nerve involvement in CKD patients (Perkins & Bril, 2014; Poernomo et al., 2003). In a study, it was noted that progressive neuropathy serves as one of the indications for initiating renal replacement therapy and is a crucial indicator of inadequate dialysis (Khafagi et al., 2022; Ramírez & Gómez, 2011).

While the prevalence of peripheral neuropathy and its associated clinical signs and symptoms has been extensively documented in various studies, there is a notable scarcity of data regarding the electrophysiological aspects of peripheral neuropathy in CKD patients within the Indonesian literature. This examination provides valuable insights into

the progression of peripheral neuropathy in CKD patients, allowing for the implementation of appropriate management strategies to prevent complications, reduce disability, and enhance the quality of life for individuals with CKD. Effective management of peripheral neuropathy in CKD patients necessitates a comprehensive approach involving various multidisciplinary fields. Motivated by this background, the researcher aims to explore and describe the nature of peripheral neuropathy in chronic kidney disease patients, considering both clinical assessments and nerve conduction examination results at Dr. Moehammad Hoesin Palembang Hospital. Hence, the primary objective of this study is to identify and characterize the manifestation of peripheral neuropathy in chronic kidney disease patients undergoing hemodialysis at Dr. Mohammad Hoesin Hospital in Palembang.

2. RESEARCH METHODS

2.1. Research Design

This study employs a cross-sectional descriptive design, utilizing primary data gathered through interviews and nerve conduction examinations (NCV) conducted with an ENMG machine. Secondary data are obtained from medical records.

The study encompasses all chronic kidney disease patients who underwent hemodialysis at Dr. Mohommad Hoesin Palembang General Hospital from May 1 to July 31, 2023. The sample consists of chronic kidney disease patients undergoing hemodialysis at Dr. Mohommad Hoesin Palembang Hospital within the specified period. Selection criteria include meeting the inclusion criteria and not falling under any exclusion criteria. The research is conducted at the Hemodialysis and ENMG Laboratory Installations of Dr. Mohammad Hoesin Hospital Palembang, spanning from May 1 to July 31, 2023.

Inclusion criteria require participants to meet the following conditions: a diagnosis of chronic kidney disease necessitating hemodialysis as per medical records; Neuropathy Symptom Score (NSS) equal to or greater than 3; age 18 or older; and willingness to participate, demonstrated by signing the research consent form. Exclusion criteria encompass patients with a recorded diagnosis of diabetes mellitus or systemic lupus erythematosus; those taking drugs causing peripheral neuropathy (e.g., chemotherapy or Isoniazid-containing tuberculosis drugs); individuals with aphasia; patients deemed unstable based on vital signs; and pregnant women.

The minimum sample size for this study was determined using the Lemeshow Formula, as follows:

$$N = \frac{(Z\alpha)^2 \times p \times q}{d^2}$$

$$N = \frac{1.96^2 \times 0.76 \times 0{,}11}{0.1^2}$$

$$N = 32.11$$

Where:
N = minimum sample size required
Z = degree of significance which is 95% (Zα = 1.96)
P = proportion of uremic neuropathy incidence in stage 5 chronic kidney disease patients(0.76)
d = limit of error or absolute precision (0.1)
q = 1-p = 0.11

Thus, the minimum sample size required for this study is 32 samples.

The research sample was obtained through consecutive sampling, selecting participants based on the sequential visits of chronic kidney disease patients undergoing hemodialysis at RSMH Palembang during the study period.

This study encompasses several variables, including age, gender, body mass index (BMI), duration of hemodialysis, potassium level, glomerular filtration rate (GFR) value, degree of peripheral neuropathy based on Neuropathy Symptom Score (NSS) value, nerve conduction examination result, and type of peripheral neuropathy lesion identified through nerve conduction examination.

The tools utilized in this study consist of the NSS scoring table and nerve conduction examination performed with the CADWELL Sierra Summit EMG & EP 6 Channel integrated Ultrasound device, manufactured in the United States in 2020.

2.2. Research Procedure

First of all, patients with chronic kidney disease undergoing regular hemodialysis at Dr. Mohammad Hoesin Palembang Hospital from May 1 to July 31, 2023, meeting the inclusion criteria and not falling under the exclusion criteria, are enrolled. Informed consent is obtained from patients, and their families receive explanations about the study's objectives, procedures, and potential side effects. Interviews collect demographic information, hemodialysis duration, and peripheral neuropathy degree based on Neuropathy Symptom Score (NSS). Data from medical records include serum potassium and creatinine levels for calculating glomerular filtration rate (GFR).

Subsequently, nerve conduction examination (NCS) is performed at the ENMG Laboratory of Dr. Mohammad Hoesin Hospital Palembang, following established Standard Operating Procedures (SPO). The study subjects are positioned comfortably in a lying position in a room maintained at a neutral temperature (26 + 2ºC). Parameters measured include:

a) Motor Nerve Conduction Study
- Parameters measured: Motor amplitude, motor distal latency, and motor nerve conduction on the Ulnar, Medianus, Tibialis posterior, and Peroneus communis Nerves.
- Electrodes placement: Surface electrodes at specific motor points with a ground electrode between the stimulus and recording electrodes.

b) Sensory Nerve Conduction Studies
- Examinations include: Sensory amplitude, sensory distal latency, and sensory nerve conduction on the ulnar, medianus, and suralis nerves.
- Electrodes placement: Recording electrodes at specific locations for each nerve.

Electrodiagnostic features are considered abnormal if two or more abnormal parameters (latency, amplitude, and NCV) are identified in NCS measurements of nerve fibers, either on one nerve or one abnormal parameter on two or more nerves.

Finally, Data collection is conducted by the researcher in the Hemodialysis Installation and ENMG Laboratory, supervised by a peripheral nerve consultant specialist at the ENMG Neurology Laboratory of Dr. Mohammad Hoesin Hospital Palembang. Abnormal and normal values in nerve conduction examination are based on the standards used in the ENMG laboratory of Dr. Mohammad Hoesin Hospital Palembang, referencing Preston (2013).

3. RESULTS AND DISCUSSION

3.1. Research Results

This study was conducted at Dr. Mohammad Hoesin Hospital in Palembang during the period from May to July 2023, utilizing primary data from all Chronic Kidney Disease (CKD) patients undergoing hemodialysis at the same hospital within the specified timeframe. The total number of chronic kidney disease patients observed from May to June 2023 was 207. After excluding patients with underlying diseases such as diabetes mellitus (DM), systemic lupus erythematosus (SLE), and those using drugs causing peripheral neuropathy like chemotherapy drugs and tuberculosis (TB) drugs containing Isoniazid (INH), 108 patients remained. Among these, 65 patients exhibited symptoms of peripheral neuropathy based on a Neuropathy Symptom Score (NSS) ≥ 3. From this subset of patients meeting the inclusion criteria and not meeting the exclusion criteria, a total of 35 patients were included in the study.

3.1.1. Distribution of CKD Patients with Peripheral Neuropathy (Uremic Neuropathy) based on Demographic and Clinical Characteristics

Table 1 presents the distribution of CKD patients with peripheral neuropathy (uremic neuropathy) according to demographic and clinical characteristics. The prevalence of uremic neuropathy, based on age, was highest in the 46-65 years age group (62.9%), followed by 18-45 years (28.6%), and over 65 years (8.6%). The youngest patient with uremic neuropathy was 21 years old, while the oldest was 70 years old, with an average age of 51.4 ± 11.4 years. Regarding gender, females (51.4%) exhibited a higher prevalence compared to males (48.6%).

In terms of BMI status, 54.3% of patients had a normal BMI, 28.6% were overweight, 14.3% were classified as obesity I, and 2.9% as obesity II. The distribution based on the duration of hemodialysis showed 45.7% of patients undergoing hemodialysis for 12-36 months, 28.6% for over 60 months, 20% for 36-60 months, and 5.7% for less than 12 months. Based on serum potassium values, 85.7% had levels ≤5.5 mEq/L, and 14.3% had levels >5.5 mEq/L. Furthermore, 85.7% of patients had GFR values <12 ml/min/1.73m², while 14.3% had GFR values >12 ml/min/1.73m².

Table 1. Distribution of CKD patients with peripheral neuropathy (uremic neuropathy) based on demographic and clinical characteristics

Variable	Total (n=35)	Percentage (%)
Age		
18-45 years	10	28,6
46–65 years	22	62,9
> 65 years	3	8,6
Gender		
Female	18	51,4
Male	17	48,6
BMI		
Underweight	0	0
Normal	19	54,3
Overweight	10	28,6
Obese I	5	14,3
Obese II	1	2,9
Duration of hemodialysis		
< 12 months	2	5,7
12-36 months	16	45,7
36-60 months	7	20,0
>60 months	10	28,6
Potassium		
≤5.5 mEq/L	30	85,7
>5.5mEq/L	5	14,3
GFR		
<12ml/min/1.73m^2	30	85,7
>12ml/min/1.73m^2	5	14,3
NSS		
Mild Degree	23	65,7
Moderate Degree	10	28,6
Severe Degree	2	5,7

The distribution of research subjects according to Neuropathy Symptom Score (NSS) revealed that 65.7% fell into the category of mild neuropathy, characterized by NSS scores of 3-4. Additionally, 28.7% exhibited moderate neuropathy, with NSS scores ranging from 5-6. A smaller percentage, 5.7%, demonstrated severe neuropathy, reflected in NSS scores ranging from 7-10.

3.1.2. Overview of Motor and Sensory Nerve Conduction Studies of CKD Patients with Peripheral Neuropathy (Uremic Neuropathy)

The motor and sensory nerve conduction examination parameters encompassed nerve conduction, amplitude, and distal latency.

1. Nerve Conduction Velocity (NCV)

Table 2 provides an overview of motor nerve NCV. For the ulnar nerve, 2.9% exhibited decreased NCV, while 97.1% were normal. In the case of the median nerve, 5.7% showed decreased NCV, with 94.3% being normal. The tibial nerve presented with 8.6% not appearing, and 91.4% being normal. Similarly, the peroneal nerve showed 8.6% not appearing, with 5.7% exhibiting decreased NCV and 85.7% being normal.

Table 2. Overview of Motor and Sensory Nerve NCV of CKD Patients with Peripheral Neuropathy (Uremic Neuropathy)

	Nerve Conduction Velocity (NCV)					
	Motor			Sensory		
	Normal	Decreased	Not Present	Normal	Decreased	Not Present
N. Ulnaris	34(97,1%)	1(2,9%)	0(0%)	3 (97,1%)	0 (0%)	1 (2,9%)
N. Medianus	33(94,3%)	2(5,7%)	0(0%)	32(82,8%)	2(5,7%)	1(2,9%)
N. Tibialis	32(91,4%)	0(0%)	3(8,6%)	N/A	N/A	N/A
N. Peroneus	30(85,7%)	2(5,7%)	3(8,6%)	N/A	N/A	N/A
N. Suralis	N/A	N/A	N/A	23(65,7%)	7(20%)	5(14,2%)

Description N/A : not available

In the examination of sensory nerve NCV, the findings are as follows: For the ulnar nerves, 2.9% did not appear, while 97.1% were normal. Regarding the median nerves, 5.7% exhibited decreased amplitude, with 82.8% being normal. The suralis nerves showed that 14.2% did not appear, 20% had decreased NCV, and 65.7% were normal.

2. Amplitude

Table 3 provides a description of the amplitude of motor nerves. It indicates that 100% of ulnar nerves have a normal amplitude, with 11.4% of median nerves exhibiting decreased amplitude and 88.6% being normal. For the tibial nerve, 8.6% did not appear, 2.9% had decreased amplitude, and 88.5% were normal. In the peroneal nerve, 51.4% showed decreased amplitude, 8.6% did not appear, and 40% had a normal amplitude.

The sensory nerve amplitude overview reveals that, in the ulnar nerve, 20% experienced a decrease, 2.9% did not appear, and 77.1% were normal. In the median nerve, 17.1% exhibited a decrease, 2.9% did not appear, and 80% were normal. Meanwhile, in the suralis nerve, 34.3% had decreased amplitude, 14.2% did not appear, and 57.1% were normal.

Table 3. Overview of Motor and Sensory Nerve Amplitude in CKD Patients with Peripheral Neuropathy (Uremic Neuropathy)

	Amplitude					
	Motor			Sensory		
	Normal	Decreased	Not Present	Normal	Decreased	Not Present
N. Ulnaris	35(100%)	0(0%)	0(0%)	27(77,1%)	7(20%)	1 (2,9%)
N. Medianus	31(88,6%)	4(11,4%)	0(0%)	28(80%)	6(17,1%)	1(2,9%)
N. Tibialis	31(88,5%)	1(2,9%)	3(8,6%)	N/A	N/A	N/A

N. Peroneus	14(40%)	18(51,4%)	3(8,6%)	N/A	N/A	N/A
N. Suralis	N/A	N/A	N/A	20(57,1%)	12(34,3%)	5(14,2%)

Description N/A : not available

3. Distal Latency

Table 4 illustrates the distal latency of motor nerves. It indicates that 100% of ulnar nerves have normal distal latency, while for the median nerve, 8.6% did not appear, and 91.4% exhibited normal distal latency. In the tibial nerve, 8.6% did not appear, and 91.4% had normal distal latency. For the peroneal nerve, 8.6% experienced lengthening in distal latency, 5.7% did not appear, and 85.7% were normal.

Regarding the distal latency of sensory nerves, 2.9% of ulnar nerves did not appear, and 97.1% had normal distal latency. In the median nerve, 2.9% did not appear, and 88.6% exhibited normal distal latency. For the suralis nerve, 14.2% of the waves did not appear, 2.9% experienced distal latency lengthening, and 68.6% had normal distal latency.

Table 4. Distal Latency of Motor and Sensory Nerves in CKD Patients with Peripheral Neuropathy (Uremic Neuropathy)

	Distal Latency					
	Motor			**Sensory**		
	Normal	Extend	Not present	Normal	Extend	Not present
N. Ulnaris	35(100%)	0(0%)	0(0%)	34(97,1%)	0(0%)	1 (2,9%)
N. Medianus	32(91,4%)	0(0%)	3(8,6%)	34(88,6%)	0(0%)	1(2,9%)
N. Tibialis	32(91,4%)	0(0%)	3(8,6%)	N/A	N/A	N/A
N. Peroneus	30(85,7%)	3(8,6%)	2(5,7%)	N/A	N/A	N/A
N. Suralis	N/A	N/A	N/A	24(68,6%)	1(2,9%)	5(14,2%)

Description N/A : not available

3.1.3. Lesion Type of CKD Patients with Peripheral Neuropathy (Uremic Neuropathy) based on Nerve Conduction Examination (NCS)

Table 5 presents the results of the Nerve Conduction Examination (NCS) in CKD patients with peripheral neuropathy. The examination revealed that 82.9% of patients experienced peripheral neuropathy, while 17.1% showed normal NCS results. In the NCS findings, sensory motor neuropathy accounted for 51.4%, sensory neuropathy for 22.9%, and motor neuropathy for 8.6%. Among these, 71.5% exhibited axonal neuropathy, 11.4% axonal-demyelinating, and no patients showed demyelinating lesions.

Table 5. Lesion Types of CKD Patients with Peripheral Neuropathy (Uremic Neuropathy) based on Nerve Conduction Examination (NCS)

Lesion Types	**Peripheral Neuropathy**			**Normal**
	Axonal	**Demyeli-nating**	**Axonal-Demyelinating**	
Motor	2(5,7%)	0(0%)	1(2,9%)	N/A
Sensory	8(22,9%)	0(0%)	0(0%)	N/A
Motor-sensory	15(42,6%)	0(0%)	3(8,6%)	N/A

Normal	N/A	N/A	N/A	6(17,1%)
Total	25(71,5%)	0(0%)	4(11,4%)	6(17,1%)

Description N/A : not available

3.1.4. Distribution of Demographic and Clinical Characteristics of CKD Patients based on Nerve Conduction Examination (NCS) Results

Table 6 illustrates the distribution of demographic and clinical characteristics of CKD patients based on the results of nerve conduction examination (NCS), focusing on the neuropathy group consisting of 29 patients (82.9%). Within this group, the age category of 46-65 years was the most prevalent, accounting for 69%, followed by 20.7% in the 18-45 years category and 10.3% in the category >65 years. Among patients with normal NCS results, the highest proportion was in the 18-45 years age category, constituting 66.7%, with 33.3% in the 46-65 years age category.

Regarding gender characteristics in the peripheral neuropathy group, 51.7% were male patients and 48.3% were female patients. Conversely, in patients with normal NCS results, 66.7% were female, and 33.3% were male.

Concerning BMI status in the peripheral neuropathy group, patients with a normal BMI comprised 55.2%, 24.1% were overweight, 17.2% were classified as obesity I, and 3.4% were classified as obesity II. In patients with normal NCS results, 50% had a normal BMI, and 50% were in the overweight BMI category.

Table 6. Distribution of Clinical and Demographic Characteristics of CKD Patients based on Nerve Conduction Examination Results (NCS)

Variable	CKD Patients	
	Peripheral Neuropathy (+) (n=29)	Peripheral Neuropathy (-) (n=6)
Age		
18-45 years	6(20,7%)	4(66,7%)
46–65 years	20(69,0%)	2(33,3%)
> 65 years	3(10,3%)	0(0%)
Gender		
Male	15(51,7%)	2(33,3%)
Female	14(48,3%)	4(66,7%)
BMI		
Underweight	0(0%)	0(0%)
Normal	16(55,2%)	3(50%)
Overweight	7(24,1%)	3(50%)
Obesitas I	5(17,2%)	0(0%)
Obesitas II	1(3,4%)	0(0%)
Duration of hemodialysis		
< 12 bulan	2(6,9%)	0(0)
12 – 36 bulan	13(44,8%)	3(50%)
36-60 bulan	5(17,2%)	2(33,3%)
>60 bulan	9(31,0%)	1(16,7%)

Potassium		
≤5.5 mEq/L	24(82,8%)	6(100%)
>5.5mEq/L	5(17,2%)	0(0%)
GFR		
<12ml/min/1.73^2	28(96,6%)	2(33,3%)
>12ml/min/1.73^2	1(3,4%)	4(66,7%)
NSS		
Mild	18(62,1%)	5(83,3%)
Moderate	9(31%)	1(16,7%)
Severe	2(6,9%)	0(0%)

Description: The majority of peripheral neuropathy is axonal, a small proportion is axonal demyelinating and there is no demyelinating.

In the peripheral neuropathy patient group, the length of hemodialysis was 12-36 months in 44.8%, >60 months in 31%, 36-60 months in 17.2%, and the length of HD <12 months in 6.9%. For patients with normal NCS results, 66.7% had a hemodialysis duration of >24 months, 16.7% had a hemodialysis duration of 12-24 months, and <12 months, respectively.

Regarding the characteristics of serum potassium results, ≤5.5 mEq/L was observed in 82.8% of patients with NCS results indicating peripheral neuropathy, while 17.2% had potassium levels >5.5mEq/L. In patients with normal NCS results, 100% had serum potassium levels ≤5.5 mEq/L.

In terms of GFR values, <12ml/min/1,732 was noted in 96.6% of patients with NCS indicating peripheral neuropathy, and 3.4% had GFR values >12ml/min/1,732. For patients with normal NCS results, 66.7% had GFR values >12ml/min/1,732, and 33.3% had GFR values <12ml/min/1,732.

Concerning the degree of peripheral neuropathy based on NSS, patients with NCS results indicating peripheral neuropathy exhibited a mild degree in 62.1%, a moderate degree in 31%, and a severe degree in 6.9%. In patients with normal NCS results, 83.3% had a mild degree, 16.7% had a moderate degree, and no patients had a severe degree.

3.2. Discussion

3.2.1. Characteristics of Peripheral Neuropathy in CKD Patients

In this study, the majority of patients fell within the age range of 46-65 years, constituting 62.9%, followed by the age range of 18-45 years at 28.6%, with an average age of 51.4 ± 11.4 years. This aligns with research by Fatima et al. (2021), where the majority of patients were in the 30-60 year category, with an average age of 55.4 ± 15.95 years. Similar trends were observed in the studies by Rizki (2022) and Gondhali et al. (2019), where the majority of samples were in the age group >50 years. Duraisamy and Parthasarathy (2018) found the most common age group to be 40-70 years, while Babu et al. (2015) noted the impact of age, especially in patients over 65 years, on peripheral neuropathy in CKD patients.

The gender distribution in this study revealed that females constituted the majority, with 51.4% (18 people), which was only slightly higher than males, accounting for 48.6% (17 people). This differs from several other studies such as those by Khafagi et al. (2022), Aggarwal et al. (2013), and Bakre et al. (2021), where men outnumbered women, with proportions of 65%, 65%, and 55.6%, respectively.

In this study, the majority of patients had a normal BMI status, accounting for 54.3% or 19 patients. Simit Doshi et al. (2019) found that a high BMI status is associated with a 2.37 times higher chance of developing new motor nerve disorders in NCV (Doshi et al., 2020). In this study, it was observed that most patients underwent hemodialysis for a duration of 12-36 months, constituting 45.7%, with an average HD duration of 50 ± 6.1 months. This aligns with the research by Gondhali et al. (2019), where 45.45% of patients had an HD duration of 12-36 months. Babu et al. (2015) also reported a similar proportion of patients (52%) with an HD duration of 12-36 months, consistent with the findings of Rathnakumar et al. (2018), where 52% of patients had an HD duration of 12-36 months. However, it contrasts with the findings of Hassan et al. (2019), who reported that 67.9% of patients had an HD duration of 12-36 months, and with Rizki (2022), who found that the duration of HD ≥ 28 months was 38.1%. Some studies have limitations on HD duration, with Duraisamy and Parthasarathy (2018) reporting an average HD duration of 6.5 ± 6.82 months, and a maximum sample duration of 24 months.

Regarding serum potassium levels, the majority in this study had levels ≤5.5 mEq/L, accounting for 85.7%, with an average serum potassium value of 4.69 ± 0.14 mEq/L, indicating normal serum potassium levels. This is consistent with research by Bakre et al. (2021), which reported an average serum potassium value of 4.79 ± 0.88 mEq/L.

In terms of GFR values, the highest proportion in this study was <12 ml/min/1.73m2, accounting for 85.7%, with an average GFR value of 7.3 ± 5.08 ml/min/1.73m2. This aligns with the findings of Fatima et al. (2021), which reported an average GFR value in the dialysis group of 10.82 ± 4.03 ml/min/1.73m2. In a study by Aggarwal et al. (2013) on predialysis patients, the average GFR value was 19.31 ± 8.10.

The distribution of research subjects based on Neuropathy Symptom Score (NSS) revealed that the majority had a mild category of neuropathy based on NSS 3-4, constituting 65.7%, with an average value of 4 ± 1.23. Supriyanto (2015) reported an average NSS score of 7.13 ± 1.85 in control and treatment groups, but there is no data on the most common NSS. Various scores, such as Michigan Neuropathy Screening Instrument Physical Assessment (MNSI), Neuropathy Disability Score (NDS), and Neurological Symptoms Score (NSS), are used to assess the initial diagnosis of neuropathy, making it challenging to find studies with the same score. For example, Bakre et al. (2021) assessed neuropathy symptoms using the NDS and found that 40% of patients experienced mild to moderate degrees of neuropathy. Aggarwal et al. (2013) reported that 70% of patients had at least one neurological symptom based on NSS. Duraisamy and Parthasarathy (2018) found that 71.66% of CKD patients undergoing hemodialysis had peripheral neuropathy based on the MSNI score.

3.2.2. Overview of Motor and Sensory Nerve Conduction Examination in CKD Patients with Peripheral Neuropathy (Uremic Neuropathy)

In this study, a motor nerve conduction examination revealed changes in latency, amplitude, and speed. Each component underwent alterations, particularly in amplitude, which exhibited a decrease and, in some cases, the absence of NCS waves. The peripheral nerve most affected by NCS changes was the common peroneal nerve, with a 54.5% decrease in CMAP amplitude. This aligns with the findings of research by D. B. Jasti et al. (2018) and M. Al-Shazly et al. (2020), where the CMAP amplitude of the peroneal nerve decreased by more than 50%, specifically 69.6% and 68.0%, respectively. However, unlike the study by Jasti et al. (2018), which identified the longest distal latency in the ulnar nerve, our study found the longest distal latency in the peroneal nerve.

The sensory nerve conduction examination depicted changes in latency, amplitude, and velocity. Each component underwent alterations, especially in amplitude, which exhibited a decrease and, in some cases, the absence of NCS waves. The peripheral nerve most affected by NCS changes was the sural nerve, experiencing a 34.3% decrease in SNAP amplitude and a 20% decrease in NCV. This is consistent with the findings of D. B. Jasti et al. (2018), where a majority of sural nerves experienced a decrease in SNAP amplitude (83.5%) and NCV (54%). Our study also aligns with M. Al-Shazly et al. (2020), reporting a 76% decrease in SNAP amplitude and a 70% decrease in NCV in the sural nerve.

In the study by Khafagi et al. (2022), lower extremity nerves (peroneal, posterior tibial, and sural) were more severely affected than upper extremity nerves, consistent with the clinical manifestations of uremic neuropathy, which typically involves the lower limbs more than the upper limbs. The obtained results are theoretically aligned with the notion that lower extremities are commonly affected first, indicating a length-dependent pattern of peripheral neuropathy in chronic kidney disease patients. Theoretically, upper extremity nerves may become involved later as kidney disease worsens (D. Jasti et al., 2017; Khafagi et al., 2022). Krishnan and Kiernan (2009) have described changes in sural sensory potentials as the most sensitive nerve conduction abnormality in CKD patients. Among various nerve conduction parameters, sural sensory amplitude is the most sensitive indicator of neuropathy in CKD, reduced in 50% of cases. Regarding the distribution of nerve affection, lower limb nerves are usually involved before upper limb nerves (D. Jasti et al., 2017).

3.2.3. Lesion Type of CKD Patients with Peripheral Neuropathy (Uremic Neuropathy) based on Nerve Conduction Examination (NCS)

Based on Table 6, the NCS examination results show that 82.9% of patients experienced peripheral neuropathy, while 17.1% had normal NCS results. This aligns with research by D. B. Jasti et al. (2018), indicating a peripheral neuropathy prevalence of 89% in CKD patients based on electrophysiological examination (NCS). Similarly, research by M. Al-Shazly et al. (2020) reported 76% of polyneuropathy cases based on NCS (ENMG) results. A review article also notes that 60 to 100% of dialysis patients experience neuropathy symptoms (Ramírez & Gómez, 2011). Several previous studies, such as Babu et al. (2015) (65%), Rathnakumar et al. (2018) (65%), and Krishnan & Kiernan (2009) (62%), have reported a prevalence of >60% peripheral neuropathy in

CKD patients based on NCS results. Bakre et al. (2021) reported 65% peripheral neuropathy and 35% normal based on NCS results (Rizki, 2022). This study demonstrates a higher incidence of peripheral neuropathy based on NCS examination compared to previous studies.

In this study, sensory-motor neuropathy (mixed) was the most common at 51.4%. This is consistent with Babu et al. (2015), who found that sensory-motor neuropathy was 34%, and Raja & Ashwinth (2020), where sensory-motor neuropathy was also 34%. However, this differs from the results of Hassan et al. (2019), who found the highest prevalence of motor neuropathy at 53.7%.

The most common type of neuropathy lesion in this study was axonal type neuropathy at 71.4%, with details showing axonal type sensory-motor neuropathy at 42.6%, followed by axonal type sensory neuropathy at 22.9%. This aligns with Sultan (2007), reporting that 42% of patients experience axonal type sensory neuropathy. Similarly, Gondhali et al. (2019) found that the most lesions were in patients with sensory-motor axonal neuropathy at 36.6%. D. Jasti et al. (2017) reported 18% experiencing axonal type sensory neuropathy. In the study by M. Al-Shazly et al. (2020), it was equally distributed, with 39.5% of patients having axonal and mixed neuropathy, respectively.

In uremic neuropathy, a length-dependent polyneuropathy where nerve conduction studies (NCS) indicate generally axonal type neuropathy, there is a decrease in sensory amplitude and often a decrease in motor amplitude. In contrast, in the early stages of the disease, patients with chronic kidney disease (CKD) show demyelinating neuropathy with prominent nerve conduction slowing and normal sensory and motor amplitude. The neuropathy that occurs is characterized by symmetrical abnormalities in the distal region, predominantly axonal neuropathy with mixed types of neuropathy (D. Jasti et al., 2017; D. B. Jasti et al., 2018).

Neurotoxins cause lesions in nerve cell bodies and axons, followed by degeneration of axon fibers distal to the lesion, a process referred to as Wallerian degeneration. This degeneration occurs because the regulation of nerve cell metabolism is in the cell body. Metabolic regulation is then passed on to more distal axons through mechanisms called anterograde and retrograde. The farther the axon is from the cell body, the easier it is for energy depletion in the axon due to uremia to occur. This results in the connection between the cell body and the distal axon being broken due to axon damage between the two. Consequently, axonal transport cannot occur, leading to the degeneration of the distal axon, which loses its mobility. If this damage persists, there will be an "axon dies back phenomenon," where the distal axon is damaged first, followed by more proximal axons. This causes symptoms characterized by weakness and sensory loss in the distal area, resembling "stocking-gloves" (Aninditha et al., 2022).

3.2.4. Distribution of Demographic and Clinical Characteristics of CKD Patients based on Nerve Conduction Examination (NCS) Results

Table 6 illustrates the distribution of demographic and clinical characteristics of CKD patients based on the results of nerve conduction examination (NCS) obtained from 29 patients in the peripheral neuropathy group. In the age category of 46-65 years, the highest proportion was observed, with 20 patients constituting 69%. Among the 6 patients

with normal NCS results, the highest proportion was in the 18-45 year age category, accounting for 66.7%.

These findings align with research by Gondhali et al. (2019), where the highest age with neuropathy was in the 45-54 year age category, while non-neuropathy patients were most prevalent in the 25-34 year age category. Bakre et al. (2021) reported that in the neuropathy group, CKD patients aged ≥35 years comprised 90%, while the non-neuropathy group was more common in CKD patients aged <35 years, constituting 60%. However, these results differ from Babu et al. (2015), which found that the majority of patients in the neuropathy group were in the 25-34 year age category.

Age-related developments can trigger changes in the metabolism of steroid hormones, namely testosterone and estrogen. The change in hormone concentration affects the functioning of mitochondria, which, in turn, has an impact on neuronal axonal transport. This is consistent with the results of Bakre et al. (2021), indicating a significant age difference in the incidence of neuropathy. However, research by Rizki (2022) and Shekar et al. (2017) found no significant relationship between age and neuropathy, possibly due to a relatively equal proportion of the sample size.

In terms of gender characteristics, the majority of patients with neuropathic NCS results were male, constituting 51.7%, compared to the group with normal NCS results. This aligns with the findings of Bakre et al. (2021), reporting that male patients with neuropathy comprised 65%. Similarly, Duraisami et al. (2018) found that men with polyneuropathy accounted for 73.8%. However, this contradicts the "Epineurim" study conducted in Colombia in 2003, which observed peripheral neuropathy occurring in 30% more women than men (Ramírez & Gómez, 2011). In the study by Shekar et al. (2017), 86.7% of polyneuropathy patients from NCS results were male, and 65% were female, although the study concluded that there was no relationship between gender distribution and the incidence of neuropathy. On the other hand, research by Duraisamy & Parthasarathy (2018) demonstrated that men were significantly more affected than women. The influence of gender on the incidence of peripheral neuropathy in chronic kidney disease patients is a complex process, and there have not been many studies directly analyzing the differences in nerve characteristics between men and women.

In this study, the highest BMI status was found in patients with NCS results indicating peripheral neuropathy, with a normal BMI status constituting 55.2%. This is nearly the same as the proportion of normal BMI status in patients with normal NCS results. Previous studies did not include variables regarding IMT status. However, in the research by Doshi et al. (2020), a high status was associated with a 2.37 times higher chance of developing new motor nerve disorders in NCV.

In this study, the majority of patients in the peripheral neuropathy group had a hemodialysis duration between 12-36 months, accounting for 44.8%. Similarly, patients with normal NCS results also had the highest proportion in the 12-36 months hemodialysis duration category, at 50%. In the research by Duraisamy & Parthasarathy (2018), patients with peripheral neuropathy were found to have a hemodialysis duration of 13-24 months, constituting 88.23%. This finding contrasts with Babu et al. (2015), where the majority of neuropathy patients were in the 36-60 months hemodialysis duration category. Hassan et al. (2019) also reported the highest prevalence of neuropathy in the 36-60 months hemodialysis duration category. Rizki (2022) found no significant

difference in hemodialysis duration between groups that experienced neuropathy and those that did not.

Regarding serum potassium levels, 82.8% of patients with peripheral neuropathy NCS results had normal potassium levels (≤5.5 mEq/L), compared to 100% of patients with normal NCS results. However, high potassium levels (>5.5 mEq/L) were found in 17.2% of patients with peripheral neuropathy NCS results, while none were observed in patients with normal NCS results. Krishnan et al. (2005) postulated that potassium contributes to uremic neurotoxicity, affecting nerve and muscle membranes. Damnjanovic et al. (2007) and Sultan (2007) also found significant correlations between potassium levels and neurophysiological parameters.

In patients with a glomerular filtration rate (GFR) value <12 ml/min/1.732, 96.6% had peripheral neuropathy NCS results, compared to 33.35% in patients with normal NCS results. Doshi et al. (2020) indicated that a lower GFR increases the likelihood of developing worse peripheral neuropathy, with a 10-unit decrease in estimated GFR associated with a 0.146 m/s decrease in nerve conduction velocity. Uremic neuropathy incidence is closely linked to kidney damage severity, with 60 to 100% of patients undergoing dialysis experiencing neuropathy symptoms when GFR falls below 12 ml/min (Ahmed et al., 2020).

According to KDOQI CKD Guidelines, below a GFR of 8-13 or a serum creatinine above 7-8 mg/dL, 50% or more of patients with decreased kidney function have abnormal nerve conduction velocities (NCV). Although the study showed a correlation between decreased GFR and NCV in CKD patients, it did not determine the threshold GFR value that reduces NCV. Urea and creatinine levels have been correlated with decreased NCV and manifestations of peripheral neuropathy (Kramer, 2010).

Additionally, the degree of neuropathy based on the Neuropathy Symptom Score (NSS) was predominantly mild, with 62.1% of patients with peripheral neuropathy NCS results and 83.3% in patients with normal NCS results. Severe degrees were found in 6.9% of patients with peripheral neuropathy NCS results but were absent in patients with normal NCS results. Zamroni et al. (2016) concluded that NSS is a validated tool that includes symptoms and signs of neuropathy, providing a quick and easy screening method in clinical practice with a high predictive value. They emphasized the importance of evaluating symptoms, which describe patients' complaints and may serve as diagnostic and prognostic indicators.

4. CONCLUSION

In conclusion, our study sheds light on the prevalence and characterization of peripheral neuropathy in chronic kidney disease (CKD) patients undergoing hemodialysis at Dr. Mohammad Hoesin Hospital Palembang. The findings underscore the significance of neurological complications in advanced CKD, affecting both central and peripheral nervous systems.

The distribution of research subjects based on the Neuropathy Symptom Score (NSS) revealed that a substantial majority, 65.7%, fell into the mild neuropathy category, demonstrating the pervasiveness of neuropathic symptoms in this population. Electrophysiology results further highlighted the prevalence of peripheral neuropathy,

with 82.9% of patients exhibiting abnormalities in nerve conduction, emphasizing the importance of electrophysiological examination (ENMG) as a diagnostic tool.

Sensory motor neuropathy was the predominant type, comprising 51.4% of cases. Among these, 71.5% exhibited axonal neuropathy, while 11.4% presented with axonal-demyelinating lesions, and no demyelinating lesions were observed. These detailed characterizations provide valuable insights into the specific types of neuropathic presentations in CKD patients.

The high prevalence of peripheral neuropathy identified in our study emphasizes the critical role of nerve conduction examination in diagnosing and monitoring neuropathic conditions in CKD patients. Early detection through electrophysiological assessment is crucial for effective management and prevention of disability complications, ultimately contributing to an enhanced quality of life for individuals with CKD. Our findings contribute to the broader understanding of neurological complications in CKD and underscore the importance of proactive neurological assessments in the care and treatment of these patients.

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