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Research Paper

Large and Small Fiber Neuropathy in Patients with Chronic Kidney Disease: A Case-Control Study from Iraq

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ABSTRACT:

BACKGROUND:

Chronic kidney disease (CKD) is associated with neurological complications, including peripheral neuropathy. While large fiber neuropathy is commonly recognized in CKD, the involvement of small fibers and the influence of arteriovenous fistula (AVF) remain less well studied.

OBJECTIVE:

This study aimed to investigate the presence of large and small fiber neuropathies in CKD patients and examine their correlation with demographic and clinical parameters.

PATIENTS AND METHODS:

This case-control study included 40 participants: 20 CKD patients on maintenance hemodialysis and 20 age- and sex-matched healthy controls. All participants underwent neurophysiological assessments, including nerve conduction studies (NCS), sympathetic skin response (SSR), and cutaneous silent period (CSP) testing.

RESULTS:

CKD patients exhibited prolonged sensory latencies (median nerve: 4.19 ± 0.49 ms vs. 3.30 ± 0.13 ms in controls; mean difference 0.89 ms, 95% CI 0.62–1.16, $p < 0.001$) and reduced SNAP amplitudes (22.03 ± 10.57 µV vs. 35.94 ± 9.05 µV; mean difference –13.91 µV, 95% CI –20.3 to –7.5, $p = 0.001$). SSR latency was prolonged and CSP latency and duration were significantly increased in the limb with AVF compared to controls and the contralateral limb.

CONCLUSION:

CKD patients on dialysis exhibit both large and small fiber neuropathy. Electrophysiological changes are more pronounced in limbs with AVF. Regular neurophysiological monitoring can aid in the early detection and management of conditions.

KEYWORDS: Chronic kidney disease, peripheral neuropathy, hemodialysis, nerve conduction studies, arteriovenous fistula.

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INTRODUCTION:

Chronic kidney disease (CKD) has emerged as a significant global health burden, affecting approximately 10% of the global population [1]. While advancements in the management of end-stage kidney disease have reduced mortality [2], CKD continues to rank among the leading causes of death and disability worldwide [3]. Beyond its established cardiovascular risks, CKD also predisposes individuals to neurological complications, partly due to the accumulation of uremic toxins. These toxins are poorly cleared by dialysis and have been implicated in both direct neurotoxicity and indirect vascular injury, contributing to cerebral endothelial dysfunction and inflammation [4,5]. Notably, recent findings indicate that neuropathy can manifest even in early stages of CKD, regardless of diabetes status [6,7]. Uremic neuropathy (UN) typically presents with distal sensory disturbances, progressing to muscle weakness and atrophy. However, clinical presentation varies, and some patients exhibit nerve dysfunction in the absence of symptoms [8]. While nerve conduction studies (NCSs) remain the gold standard for diagnosing large fiber neuropathy, they often lack the sensitivity to detect early or asymptomatic cases [9]. Moreover, small fiber neuropathy may be underrecognized, especially in diabetic CKD patients [10]. Differentiating neuropathic from myopathic presentations and ruling out alternative etiologies, such as glucose dysmetabolism or connective tissue disease, are essential components of accurate diagnosis [11].

In addition to systemic uremic neuropathy, dialysis-related factors may exert localized effects on nerve function. The arteriovenous fistula (AVF), while considered the gold standard for vascular access, alters regional hemodynamics, increases venous pressure, and may compromise neural microcirculation in the ipsilateral limb. These changes can predispose patients to focal neuropathic alterations that are distinct from generalized uremic neuropathy [12]. Investigating AVF-related differences is therefore essential for understanding the full spectrum of neurological complications in CKD.

Despite extensive documentation of large fiber involvement, the prevalence and clinical correlates of small fiber neuropathy in CKD patients remain insufficiently studied, particularly in non-Western populations. This study aims to investigate the presence and patterns of both large and small fiber neuropathies in patients with CKD in Iraq, and to assess their associations with key demographic and clinical variables.

PATIENTS & METHODS:

Study design

A case-control study was conducted at the Neurophysiology Department of Al-Imamian Al-Kadhimyian Medical City in Baghdad from March 2024 to December 2024. Twenty patients with CKD were diagnosed and managed by a Senior Nephrologist. They were on three-times/week hemodialysis sessions at the Dialysis Unit at Al-Imamain Al-Kadhimain Medical City, Baghdad, Iraq. Another 20 age- and sex-matched healthy individuals served as the control group. The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure transparent reporting [13].

Eligibility Criteria

Participants were eligible for inclusion if they were of either sex, aged between 18 and 60 years, and undergoing maintenance hemodialysis for a duration exceeding three months. Individuals were excluded if they had a history of polyneuropathy due to any cause, such as diabetes mellitus, hypothyroidism, vitamin B12 deficiency, or chronic alcoholism. Additional exclusion criteria included the presence of previously nonfunctioning arteriovenous fistulae (AVF), psychiatric illnesses, systemic inflammatory or malignant diseases, and the use of medications known to affect peripheral nerves or the autonomic nervous system.

The sample size of 20 patients and 20 controls was chosen based on a priori estimation that this number would provide approximately 80% power to detect large effect sizes ($d \approx 0.8$) at a two-sided significance level of 0.05.

Control subjects were screened through detailed history, physical examination, and basic laboratory tests to exclude diabetes, thyroid disease, vitamin B12 deficiency, alcohol use, and other systemic illnesses. Furthermore, nerve conduction studies were performed to ensure the absence of subclinical neuropathy before inclusion

History and Clinical Examination

All patients were referred by senior nephrologists. They underwent physical examinations and took a clinical history and questionnaires that included age, sex, weight, height, side of fistula, duration of hemodialysis, and the cause of end-stage kidney disease. Routine blood tests included CBC, blood urea, serum creatinine, parathormone, ferritin, iron, vitamin D, and calcium levels. Hemodialysis Technique is performed three times per week. The dialysis sessions last 3-4 hours, using conventional heparin. Vascular access was through an arteriovenous fistula. The dialyzer used was a high-flux poly-sulfone with a membrane surface area appropriate for each patient. The blood flow rate was 300-350 mL/min, with a dialysate flow rate of 500 mL/min.

Electrophysiological Studies

Using a Keypoint EMG machine (Medtronic, Denmark) to test peripheral nerves and perform autonomic studies. Surface recording electrodes (H690 NM-317Y3, DK-2740, Denmark), a grounding electrode (H658NM-550B, disk type, DK-270, Denmark), and a bipolar surface stimulating electrode (H690NM-317Y3, DK-2740, Denmark) were used. The ambient temperature was around 25°C, and skin temperature was maintained between 32°C and 34°C. Following Preston and Shapiro's methods, electrophysiological tests included sensory nerve conduction (SNC) for the right median, ulnar, radial, and sural nerves on both sides, and motor nerve conduction (MNC) for the median, ulnar, peroneal, and tibial nerves. Recordings were taken from specified muscles, and the right sural/radial amplitude ratio (SRAR) was measured [14]. The Cutaneous Silent Period test was done on the arm with AVF and compared to the contralateral side. The cutaneous silent period (CSP) was provoked by electrical square pulse stimulation using standard bipolar electrodes. Electrical stimuli were applied to the second finger of the participants, with square wave pulses of 0.5 milliseconds (in duration), at an intensity of 56 to 80 mA (from 14 times above

the sensory threshold) and at a frequency of 3 Hz. Individuals were asked to perform maximum voluntary contractions during the electrical stimuli. Five recordings were made at 30-second intervals.

To record the sympathetic skin response (SSR), the area was cleaned, and surface electrodes were used. The active electrode was placed over the right palm and sole, the reference on the dorsal aspect of the right palm and sole, and the ground on the right arm and leg. A 0.1 msec, 10 mA electrical stimulus was delivered to the contralateral median and tibial nerves at the left wrist and medial malleus with single 200 ms square pulses at irregular intervals. Skin temperature was maintained between 34°C and 35°C during testing.

Statistical Analysis

Statistical analyses were conducted using SPSS software version 25.0 (SPSS, Chicago). Continuous data were tested for normality using the Shapiro-Wilk test. Data with a normal distribution were presented as mean and standard deviation and analyzed with the Student's t-test. Categorical variables were expressed as numbers and percentages and analyzed with the Chi-square test. Pearson's correlation analysis was used to examine relationships between different quantitative variables with a two-tailed test. A p-value less than 0.05 was considered statistically significant. Given the exploratory design and small sample size, no formal adjustment for multiple comparisons (e.g., Bonferroni correction) was applied.

Ethical Statement

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from the Iraqi Board for Medical Specialization (Order No. 626, dated 30/01/2024). All participants received detailed information regarding the study objectives, procedures, and potential risks, and written informed consent was obtained from each participant prior to enrollment.

RESULTS:

Demographic and Clinical Data

The age and sex were similar between the patients and controls. The hemodialysis duration was 33.15±18.43 months. The eGFR was 9.15±7.14 mL/min/1.73 m². Eighteen (90%) of CKD patients were classified as stage 5. Eleven (55%) of patients had right-sided AVF and 9 (45%) had left-sided AVF. Fourteen (70%) of patients had hypertension (**Table 1**).

Table 1: Demographic data of the study population

Parameter	Patients (n=20)	Controls (n=20)	p-value
Age (years)	50.65 ± 11.9	48.7 ± 11.2	0.597
Sex, n (%)			0.723
Male	15 (75%)	14 (70%)	
Female	5 (25%)	6 (30%)	
Hemodialysis duration (months)	33.15 ± 18.43	–	–
eGFR (ml/min/1.73m²)	9.15 ± 7.14 (range: 4–34)	–	–
CKD Stage, n (%)			–
Stage 5	18 (90%)	–	
Stage 4	1 (5%)	–	
Stage 3b	1 (5%)	–	
Causes of CKD, n (%)			–
Hypertension	14 (70%)	–	
Unknown	3 (15%)	–	
Renal agenesis	1 (5%)	–	
Covid-19	1 (5%)	–	
Polycystic kidney disease	1 (5%)	–	
Frequency of hemodialysis /week	2.80 ± 0.52	–	–
Comorbid Disease, n (%)			–
None	16 (70%)	–	
Covid-19	4 (30%)	–	
Fistula Side, n (%)			–
Right	11 (55%)	–	
Left	9 (45%)	–	

Hematological and biochemical data of Patients with CKD

The rheological and biochemical data, including renal function tests, serum electrolytes, liver function tests, vitamin D and parathyroid hormone level were presented in **Table 2**.

Table 2: Blood Rheology and Biochemistry of the Patient Group.

Parameter	Value	Normal values
Rheological		
Hemoglobin, gm/dL	10.53±1.54	13 – 17.5
Platelet count ×1^9/L	171.50±65.51	125 – 350
WBC count ×10^9/L	5.65±2.10	3.5 – 9.5
Serum Ferritin, ng/mL	406.81±232.29	70 – 435
Total Iron, µg/dL	86.16±33.99	40- 155
TIBC, mg/dL	292.07±81.73	250- 400
UIBC, µg/dL	206.56±96.68	111- 343
Serum Electrolytes		
Potassium, Mmol/L	5.39±0.76	4.1 – 4.78
Calcium, mg/dL	8.55±0.63	8.5 – 10
Sodium, Mmol/L	139.76±3.83	136 – 145
Phosphorus, mg/dL	5.11±1.46	2.5 - 5
Renal Function Tests		
Blood Urea, mg/dL	117.11±27.79	10 – 50
Serum Creatinine, mg/dL	8.20±2.93	0.9 – 1.3
Total Serum Protein, gm/dL	4.13±0.20	6-8.5
Serum Albumin, gm/dL	6.72±0.48	3.5-5
Liver Function Tests		
Alkaline Phosphatase, U/L	310.80±127.55	98 - 279
Alanine Transaminase, U/L	15.49±6.09	0 - 40
Aspartate Aminotransferase, U/L	17.26±10.92	0 - 40
Vitamin D, ng/mL	14.85±6.66	20 – 100
Parathyroid hormone, Pg/mL	422.04±230.44	9.2-44.6

Nerve conduction study

The SLs of the sural, bilateral median, and right ulnar nerves were significantly prolonged in the patients compared to the controls (p = 0.016, p < 0.001, and p = 0.006, respectively). On the contrary, the SNAP amplitude values of the patients were significantly lower for the median and ulnar nerves bilaterally (p = 0.001, p < 0.001, p = 0.011, and p = 0.039, respectively). Regarding the sensory conduction velocity (SCV), the sural, radial, median, and ulnar nerves bilaterally were reduced in the patient group relative to the controls (p = 0.005; p = 0.004; p <0.001; and p = 0.0007, respectively) as shown in **Table 3**.

Table 3: Sensory Nerve Conduction Study.

Nerve/Parameter		Controls (n=20)	Patients (n=20)	P-value	95% CI Lower-upper	Effect size
Sural	SL, ms	3.5±0.47	4.37±0.57	0.016	1.475-0.17003	1.665396
	SNAP amplitude, µV	16.75±1.71	10.54±6.50	0.080	0.8131-13.229	1.306658
	SCV, m/s	46.8±5.71	41.61±1.87	0.005	1.798-8.567	1.221582
Radial	SL, ms	2.36±0.33	2.60±0.49	0.144	0.5514-0.841	0.574531
	SNAP amplitude, µV	25.42±5.71	20.45±11.89	0.171	2.268-12.207	0.532876
	SCV, m/s	61.09±10.33	51.39±7.52	0.004	3.3613-16.021	1.073613
SRAR		0.70±0.07	0.48±0.28	0.196	0.12502-0.5656	1.077991
Rt. Median	SL, ms	3.3±0.13	4.19±0.49	<0.001	1.1619-0.6264	2.482781
	SNAP amplitude, µV	35.94±9.05	22.03±10.57	0.001	6.581-21.2236	1.413705
	SCV, m/s	53.83±3.86	44.70±6.04	<0.001	5.4096-12.8437	1.80129
Lt. Median	SL, ms	3.27±0.14	4.18±0.67	<0.001	1.2973-0.51924	1.880189
	SNAP amplitude, µV	36.01±6.85	20.72±9.53	<0.001	8.7472-21.8361	1.842413
	SCV, m/s	56.41±7.11	45.01±5.75	<0.001	6.6754-16.1255	1.763107
Rt. Ulnar	SL, ms	3.03±0.33	3.39±0.39	0.006	0.6134-0.10817	0.996546
	SNAP amplitude, µV	26.21±6.50	17.54±10.99	0.011	2.1258-15.2065	0.960285
	SCV, m/s	54.36±3.66	47.17±4.30	<0.001	4.4066-9.5726	1.800722
Lt. Ulnar	SL, ms	3.06±0.14	3.33±0.44	0.060	0.54939-0.1202	0.826961
	SNAP amplitude, µV	32.92±6.45	22.15±14.84	0.039	0.5595-20.973	0.941288
	SCV, m/s	57.81±8.08	49.07±7.75	0.007	2.561-14.9275	1.103993

None of the common peroneal parameters differed between the two groups. The DMLs of the median and ulnar nerves bilaterally were prolonged in CKD patients (p < 0.001; p = 0.006; and p = 0.029, respectively). Moreover, the CMAP amplitudes of the median nerve bilaterally and the tibial nerve were significantly reduced (p = 0.034; p = 0.022; p = 0.001; respectively) in the patients compared to control values. Regarding the MCVs, they were significantly reduced in the patients versus the controls for median and ulnar nerves bilaterally (p < 0.0001; p = 0.0009; p = 0.001; and p = 0.002, respectively), as shown in **Table 4**.

Table 4: Motor Nerve Conduction Study.

Nerve/Parameter		Controls (n=20)	Patients (n=20)	P-value	95% CI Lower-upper	Effect size
Rt. Median	DML, ms CMAP amplitude, mV MCV, m/s	3.36±0.39 9.23±5.4 60.44±5.01	4.67±1.29 5.90±3.47 51.64±4.90	<0.001 0.034 <0.001	1.9929-0.6257 0.26061-6.4089 4.6613-12.934	.374689 0.733679 1.775874
Lt. Median	DML, ms CMAP amplitude, mV MCV, m/s	3.24±0.50 10.36±5.43 62.06±8.92	4.29±0.74 6.43±3.66 52.84±4.20	<0.001 0.022 0.009	1.5311-0.5592 0.59951-7.2634 2.5225-15.9163	1.662692 0.848746 1.322509
Rt. Ulnar	DML, ms CMAP amplitude, mV MCV, m/s	2.69±0.57 7.88±2.78 62.48±6.78	3.21±0.48 6.21±3.46 51.98±6.40	0.006 0.131 0.001	0.88063-0.15831 0.52240-3.85510 4.7699-16.2370	0.986858 0.532106 1.5926610.
Lt. Ulnar	DML, ms CMAP amplitude, mV MCV, m/s	2.65±0.51 9.08±3.54 64.25±5.84	3.05±0.38 6.81±3.63 52.10±8.01	0.029 0.131 0.002	0.75300-0.04524 0.72359-5.26698 5.2066-19.0984	0.889438 0.633144 1.733366
Common Peroneal	DML, ms CMAP amplitude, mV MCV, m/s	4.23±1.05 4.27±0.93 47.45±2.95	4.7±0.98 3.18±1.80 45.71±4.78	0.310 0.175 0.411	1.44440-.47949 0.51803-2.68505 2.56135-6.05082	0.462779 0.760835 0.438085
Tibial	DML, ms CMAP amplitude, mV MCV, m/s	4.70±1.00 8.30±1.34 46.43±4.63	4.94±1.08 4.89±2.02 43.19±3.33	0.631 0.001 0.067	1.27142-.78721 1.57550-5.23713 0.25196-6.73968	0.230599 1.989429 0.803426

Sympathetic Skin Response

The palmar SSR latency was significantly prolonged (p = 0001 and p = 0.003, respectively) in the patients with CKD, whether the side with or without AVF. For the planter SSR, the latency was prolonged and the amplitude was reduced in patients versus the control group (p <0.0001) as shown in **Table 5**.

Table 5: Sympathetic Skin Response of the Study Population.

Sympathetic Skin Response		Patients (n=20)	Controls (n=20)	P-value	95% CI Lower-upper	Effect size
Limb with AVF	Latency, sec Area, mVs Amplitude, mV	2.21±0.45 2.81±2.2 2.40±1.87	1.36±0.20 4.02±2.21 3.51±2.18	0.001 0.108 0.104	1.07920-0.62880 0.27997-2.70844 0.23738-2.45138	2.441058 0.548751 0.546549
Limb without AVF	Latency, sec Area, mVs Amplitude, mV	1.74±0.35 4.25±3.57 3.35±2.48	1.39±0.13 3.79±1.67 3.55±1.49	0.003 0.458 0.794	0.54842-0.15143 2.65121-1.74406 1.33484-1.73032	1.32572 0.165057 0.097762
Planter	Latency, sec Amplitude, mV	2.60±0.38 0.51±0.18	2.08±0.31 3.30±1.33	<0.001 <0.001	0.76504-0.27142 2.02841-3.54751	1.499549 2.939857

Cutaneous Silent Period

The CSP latencies 1 and 2 were significantly prolonged (p = 0.001 and p <0.001, respectively) in the upper limb with AVF of the patient group. Similarly, they were significantly longer (p = 0.003; p = 0.001, respectively) in the patient group in the upper limb without AVF. Furthermore, the CSP duration of the upper limb with AVF was significantly prolonged when compared to the control values (p = 0.001)

Analysis within the patient group

Only the peak SL of median N was significantly longer (p 0.021) and the ulnar CMAP amplitude was significantly lower (p = 0.036) in the side with AVF in comparison to the side without AVF. Considering SSR comparison within the patient group, only the latency was significantly longer in the side with AVF when compared to the side without AVF (p = 0.002). With respect to CSP, only the CSP latency two was significantly prolonged in the upper limb with

AVF when compared to the limb without AVF (p = 0.048).

Correlation analysis

The current study reveals no significant correlation between disease duration, laboratory blood indices, eGFR, and CKD staging and electrophysiological parameters. The right median SNAP and ulnar SNAP amplitudes bilaterally were positively correlated with hemodialysis duration (r = 0.564; p = 0.018, r = 0.632; p = 0.004, and r = 0.499; p = 0.035, respectively) as indicated in **Figure 1**.

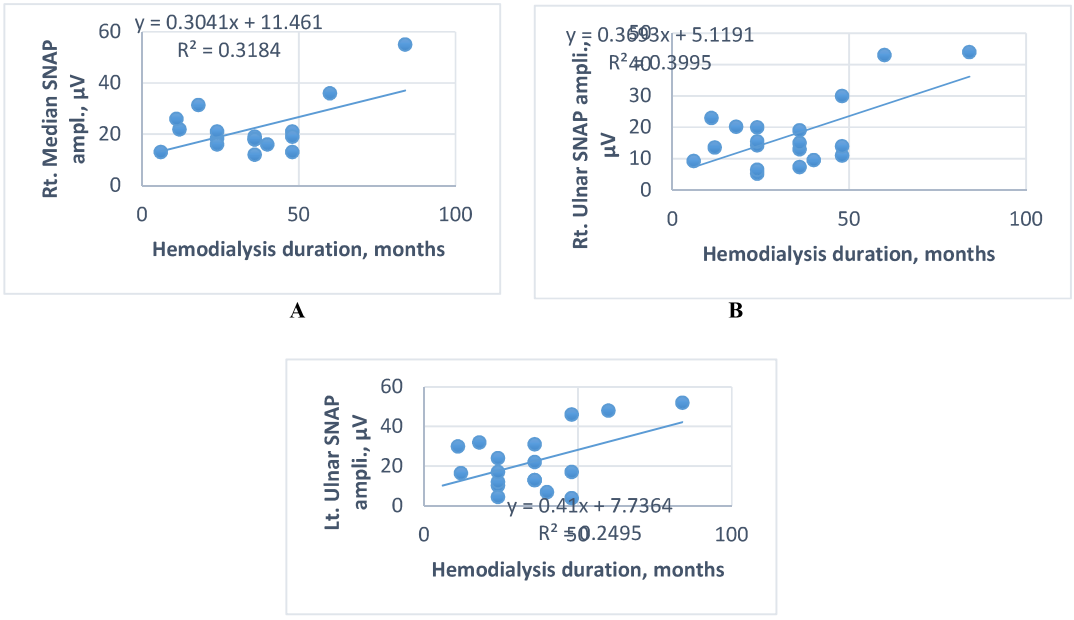

Figure 1: Association between hemodialysis duration and SNAP amplitudes in the patient group.
A: Scatter plot and regression line between hemodialysis duration and right median SNAP amplitude within the patient group
B: Scatter plot and regression line between hemodialysis duration and right ulnar SNAP amplitude within the patient group
C: Scatter plot and regression line between hemodialysis duration and left ulnar SNAP amplitude within the patient group

A positive relationship was found between CSP duration and median DML (r = 0.496; p = 0.037). Similarly, CSP2 latency was positively correlated with median DML (r = 0.681; p = 0.002) as shown in **Figure 2**.

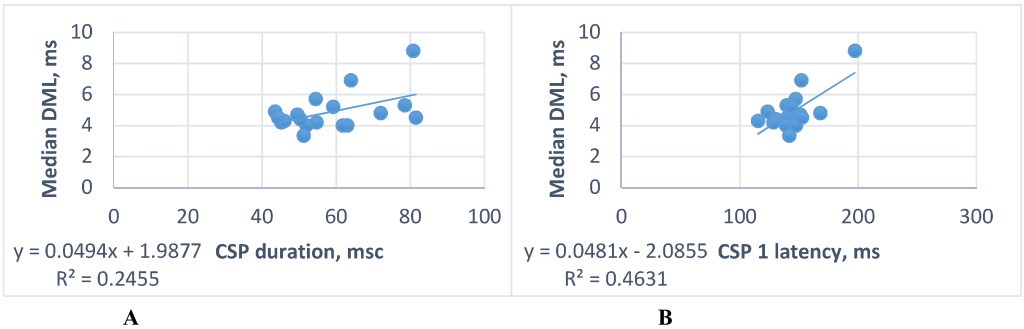

Figure 2: Correlation between CSP parameters and DML in the limb with AVF.
A: Scatter plot and regression line between CSP duration and median DML in the limb with AVF
B: Scatter plot and regression line between CSP 1 latency and median DML in the limb with AVF

The median SCV was positively correlated with palmar SSR latency (r = 0.604; p = 0.010), palmar SSR area (r = 0.654; p = 0.006), and palmar SSR amplitude (r = 0.595; p = 0.012). Also, the ulnar SNAP amplitude was positively correlated with palmar SSR latency (r = 0.536; p = 0.027), palmar SSR area (r = 0.497; p 0.050), and SSR amplitude (r = 0.589; p = 0.013).

DISCUSSION:

This investigation delineates electrophysiological alterations in patients with CKD undergoing hemodialysis, indicative of sensorimotor peripheral neuropathy, primarily of an axonal nature with secondary demyelination. Such findings are corroborated by similar reports globally. An Indian study involving 100 CKD patients observed nerve latency prolongation, diminished nerve amplitude, and reduced NCV, predominantly among dialysis patients. Another Indian investigation encompassing 200 pre-dialysis CKD patients documented significant alterations in median and ulnar SCVs and SNAP amplitudes, though not in sural nerves, excluding tibial and peroneal nerves [14-16]. In Pakistan, a study of 60 individuals revealed that median and sural nerve latencies were significantly increased, whereas amplitude and velocity were decreased compared to control subjects ($p < 0.05$) [17]. A United Kingdom study involving 15 CKD patients with a mean age of 56. 88 ± 2. 53 years and 15 controls identified that sural (P = 0. 04), peroneal (P = 0. 002), and tibial (P = 0. 007) NCVs, as well as tibial nerve amplitude (P = 0. 03), were markedly lower in the patient cohort [18]. The study finds a significant positive correlation between hemodialysis duration and median and ulnar SNAP amplitudes, consistent with other research linking neuropathy to dialysis duration [19-21]. However, there is no significant correlation between disease duration, blood indices, and electrophysiological parameters.

CKD patients on hemodialysis exhibit not only large fiber neuropathy but also clear evidence of small fiber involvement, as shown by prolonged CSP and SSR abnormalities. These findings expand upon earlier reports that largely focused on large fibers alone. Furthermore, we provide evidence that the presence of an AVF is associated with asymmetrical electrophysiological changes, suggesting a localized vascular or hemodynamic contribution to neuropathy. This observation is clinically relevant, as it emphasizes the need to monitor the fistula-bearing limb in dialysis patients more carefully and may inform future strategies for vascular access planning.

The palmar SSR latencies were abnormally prolonged in the upper limb, both with and without AVF, compared to controls. Similarly, the plantar SSR latency was extended, with a lower amplitude observed in patients. These findings are consistent with those reported in other studies. A Korean study involving SSR in patients undergoing hemodialysis, aged 26 to 67, found that SSR was absent in four patients (26.7%) and identified no significant correlation between SSR and autonomic symptoms ($P>0.05$). SSR was absent in two of seven patients with normal NCS, with no relationship between NCS and SSR ($P>0.05$) [22]. A Spanish study involving 19 patients on chronic hemodialysis, before and after a single session, demonstrated an increase in amplitude following dialysis with cellulose membranes (994±1015 vs. 382±465 μV, $p < 0.05$), although there was no change in latency. Dialysis using non-cellulosic membranes did not affect amplitude or latency [23].

In this study, CSP latencies 1 and 2 were markedly extended in patients with CKD, whether recorded from the upper limb with or without AVF, likely attributable to a reduction in small nerve fibers. In our cohort, no correlation with CKD stage or eGFR was observed. This likely reflects the predominance of stage 5 patients, creating a restricted range ('floor effect') and reducing variability. Moreover, uremic neuropathy is multifactorial, with contributors such as toxins, vascular changes, and metabolic disturbances acting independently of eGFR. Recent studies also show that neuropathy may persist after transplantation or that sudomotor dysfunction is not independently linked to eGFR, supporting our findings [24, 25].

Limitations

The small sample size may limit generalizability and statistical power to detect subtle associations. Although diabetic patients were excluded to isolate CKD effects, subclinical glucose abnormalities couldn't be fully ruled out. The cross-sectional design prevents causal inferences or tracking neuropathy over time. Advanced tests, such as skin biopsy or sensory testing, were not used, which may have led to an underestimation of small fiber neuropathy. AVF side comparisons were made; however, factors such as limb dominance and vascular flow were not controlled.

Furthermore, the relatively small sample size reduces statistical power, particularly for detecting modest associations, and increases the chance of type II error. The single-center, hospital-based recruitment may also introduce

selection bias, as patients from one tertiary care unit may not fully represent the broader CKD population. These factors limit the generalizability of our findings and underscore the need for larger, multicenter studies.

CONCLUSION:

This study found that large-fiber sensorimotor neuropathy, primarily axonal in nature, is a common neurological finding among patients with CKD on hemodialysis. Electrophysiological testing revealed abnormalities in both small and large fibre nerve conduction, with more pronounced changes observed as the severity of CKD increased. Additionally, side-to-side differences were noted between limbs with and without AVF. However, no clear association was identified between the electrophysiological findings and clinical variables, such as CKD stage, eGFR, blood indices, or disease duration. Regular neurophysiological monitoring may be advisable for hemodialysis patients to detect early neuropathic changes. Larger studies are needed to better understand the impact of clinical and laboratory variables on neuropathy progression and to validate the use of periodic electrophysiological screening.

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Author Contributions: The 1st author conceived and designed the study, collected and analyzed the data, and drafted the manuscript. The 2nd and 3rd authors supervised the research process, provided critical revisions, and approved the final version of the manuscript.

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