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A Clinical and Electrophysiological Study of Peripheral Neuropathies in Predialysis and Dialysis Patients: Our Experience from South India

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Abstract

Objective: To study the prevalence, clinical features, electrophysiological features and severity of peripheral neuropathy in chronic kidney disease (CKD) patients.

Material and methods: Between May 2015 and December 2016, 200 CKD patients and 25 controls were assessed prospectively.

Results: Prevalence of peripheral neuropathy in CKD patients was 50% based on clinical symptoms and 89% based on electrophysiological studies. Mean age of 200 CKD patients was 54.1 ± 11.9 years. 135 (67.5%) were male and 65 (32.5%) were female. Mean duration of disease was 4.2 ± 3.7 years. Positive sensory, negative sensory and autonomic symptoms were seen in 97(48.5%), 77(38.5%) and 17(8.5%) patients respectively. Symptomatic neuropathy was common in peritoneal dialysis patients. Definite and early damage was seen in 133 (66.5%) and 45 patients (22.5%) respectively, while 22 patients (11%) had no significant peripheral neuropathy. In predialysis patients (n=100); 63 (63%) had definite damage and 24(24%) had early damage. In peritoneal dialysis patients (n=50); 34(68%) had definite damage and 8(16%) had early damage. In hemodialysis patients (n=50); 36(72%) had definite damage and 13(26%) had early damage. Hemodialysis group (98%) showed more severe peripheral neuropathy. Most common nerves involved were sural, ulnar sensory, median sensory, common peroneal and posterioir tibial in CKD. Axonal and mixed sensorimotor neuropathy patterns were most common patterns in CKD.

Conclusion: Peripheral neuropathy is common in CKD with highest prevalence and severity in hemodialysis group. Symptomatic peripheral neuropathy is common in peritoneal dialysis group. Newer treatment modalities are required to manage uremic neuropathy in early stage.

Introduction

Chronic kidney disease (CKD) is a global health problem, as it leads to decreased eminence of life and it's a major perturb of developing countries. In western countries, diabetes and hypertension account for over 2/3rd of the cases of CKD.[1] In India too, diabetes and hypertension today account for 40–60% cases of CKD.[2] The patients with CKD are commonly jeopardized for morbidity and mortality as they are exposed to several complications of the disease. One of the most common triggered complications of uremia is peripheral neuropathy. In order to establish the extent of peripheral nerve involvement in patients with uremia, the function of peripheral nerve is studied by nerve conduction studies. Distal symmetrical sensorimotor peripheral neuropathy is more common and it primarily affects the lower limbs more than the upper limbs. Even though there are advancements in the treatment of uremia, uremic neuropathy often fails to respond to available treatment options.

The uremic neuropathy was suspected by Charcot in 1880[3] and then by Osler in 1892. In 1962, the detailed explanation regarding the pathologic and clinical features was given by Asbury, Victor and Adams.[4] The present concept of uremic neuropathy was established by Dyck and his colleagues in 1971.[5]

Electrophysiological studies in adults demonstrated that almost 80% of CKD patients had electrophysiological signs of impaired nerve function, although only one half of these patients were symptomatic.[6-8] According to study by Nielson et al in 1971, Danish patients with CKD were found to have 77% symptoms and 51% signs of clinical neuropathy.[9] The pathologic features of peripheral neuropathy in patients of CKD are striking axonal degeneration in the most distal nerve trunks with secondary segmental demyelination. The condition has a predilection for large diameter axons. Neuropathy is certainly multifactorial in uremia, in that it is exacerbated by hypomagnesaemia, hypocalcaemia and nutritional deficiency. Various 'uremic toxins' have been proposed in the pathogenesis of uremic neuropathy, including guanidine compounds, particularly methyl guanidine,[10] polyamines, phenol metabolites and myoinositol. Marked elevations in the concentrations of middle molecules have been demonstrated in CKD patients, a finding not observed in healthy controls, which was also proposed in the pathogenesis of uremic neuropathy.[11] Examples of such molecules include parathyroid hormone (PTH) and β-2 microglobulin,

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Table 1: Motor nerve conduction studies: standardized normal adult values in both upper and lower extremities[13]

Nerve	Record	Amplitude (mV)	Conduction velocity (m/sec)	Distal latency (millisec)
Median	APB	>6	>49	<4.4
Ulnar	ADM	>6	>49	<3.3
Common peroneal	EDB	>4	>44	<4.5
Posterior tibial	AH	>5	>41	<4.5

APB= abductor pollicis brevis; ADM = abductor digiti minimi; EDB = extensor digitorum brevis; AHB = adductor hallucis.

Table 2: Sensory nerve conduction studies: standardized normal adult values in both upper and lower extremities[15]

Nerve	Recording site	Amplitude (mV)	Conduction velocity (m/sec)	Distal peak latency (millisec)
Median	Wrist	>10	>50	<3.5
Ulnar	Wrist	>10	>50	<2.5
Sural	Ankle	>10	>45	<3.0

the levels of which are elevated in patients with CKD.

Data regarding prevalence, patterns and severity of peripheral neuropathy in various stages of CKD is sparse in Indian literature. There was no significant contribution from Indian literature regarding uremic neuropathy. This present study was done to assess the clinical and electrophysiological prevalence of peripheral neuropathy in patients of CKD with special emphasis on electrophysiological parameters and severity of peripheral neuropathy.

Material and Methods

During the period May 2015 to December 2016, 200 consecutive patients diagnosed to have and treated for CKD at Sri Venkateswara Institute of Medical Sciences, Tirupati were included in the present study. CKD patients include predialysis patients, peritoneal dialysis patients and hemodialysis patients. Patients with preexisting peripheral neuropathy prior to the diagnosis of CKD were excluded from the present study. The study was approved by the institutional ethics committee and written informed consent was obtained from the patients for their participation in the study. 25 healthy controls who gave consent to participate were included in the study.

Study Procedure

200 consecutive CKD patients who had given consent to participate in the study were divided into three groups. Group 1 included 100 pre-dialysis CKD patients with serum creatinine more than 2 mg/dL, but not initiated on dialysis. Group 2 included 50 patients who were on peritoneal dialysis. Group 3 included 50 patients who were on maintenance hemodialysis. 25 healthy volunteers were taken as controls.

Detailed history was elicited pertaining to symptoms of peripheral neuropathy. Detailed general physical examination and neurological examination were done and documented. Biochemical investigations including blood urea, serum creatinine and serum electrolytes were measured in all the patients as per the standard methods used in the department of biochemistry.

Nerve conduction studies

Both cases and controls were subjected to nerve conduction studies (NCS) using medelec synergy and natus machines. NCS procedure was done for both motor conductions and sensory conductions. Median nerve, ulnar nerve, common peroneal nerve and posterior tibial nerve were assessed for motor conductions. Median nerve, ulnar nerve and sural nerve were assessed for sensory conductions. In motor conductions; distal latency, conduction velocity, amplitude and F wave were assessed. In sensory conductions; distal latency, conduction velocity and amplitude were assessed.

Only right upper limb parameters were used in patients, because many dialysis patients who participated in the study had arteriovenous fistula on their left upper limb. So to standardize the values, we considered the parameters of right upper limb only in both cases and controls. In lower limbs sensory and motor conductions were done in both the lower limbs.

Motor nerve conduction studiesprocedure[12]

The gain was normally set at 2 to 5millivolts per division for the motor conduction studies. The recording electrodes were placed on the muscle being studied. The belly-tendon montage was used commonly. The center of the muscle belly (over the motor endplate) was used for placing the active recording electrode (also known as G1) and the reference electrode (also known as G2) was placed distally, over the tendon of the muscle. The nerve that supplies the muscle was used for placing the stimulator, where the cathode was placed close to the recording electrode. The duration of the electrical pulse was generally set to 200 milliseconds for the motor nerve conduction studies. In order to achieve supramaximal stimulation, current in the range of 20 to 50 milliamperes (mA) was used. The underlying nerve fibers were brought to action potential as the current was steadily increased from a baseline, usually by 5 to 10mA. The summation of all the underlying individual muscle fiber action potentials was represented by the compound muscle action potential (CMAP). When all the nerve fibers have been excited and the supramaximal stimulation has been achieved then the CMAP shall no longer increase in size.

For median nerve motor conduction studies, the recording electrode was placed over the motor point of the abductor pollicis brevis muscle, at the midpoint of a line drawn from the first metacarpophalangeal joint to the insertion of the tendon of the flexor carpi radialis muscle and the reference electrode was placed over the distal interphalangeal joint. Mid arm, antecubital fossa and wrist were sites of stimulation for median nerve motor conduction studies. For ulnar nerve motor conduction studies, the recording electrode was placed over the motor point of the abductor digiti minimi muscle, at the midpoint of a line between the fifth metacarpophalangeal joint and the pisiform bone, with the reference electrode over the middle phalanx of digit V. Axilla, above elbow, ulnar groove and medial wrist were sites of stimulation for ulnar nerve motor conduction studies. For the posterior tibial nerve, the CMAP was recorded by placing the active electrode over the middle of the adductor hallucis muscle, and the reference electrode over the proximal phalanx of digit I. The posterior tibial nerve was stimulated below the medial malleolus and in the popliteal fossa. For common peroneal nerve motor conduction studies, the recording electrode was placed in the middle of the extensor digitorum brevis muscle. The common peroneal nerve

Table 3: Comparison of symptoms and signs of 200 CKD patients, 100 predialysis patients, 50 patients in peritoneal dialysis group and 50 patients in hemodialysis group

Symptoms and signs	Patients (n = 200)	Predialysis cases (n = 100)	Peritoneal dialysis group (n = 50)	Hemodialysis group (n = 50)	p value
Motor weakness	6 (3%)	0 (0%)	6 (12%)	0 (0%)	<0.001
Sensory symptoms					
Positive symptoms	97 (48.5%)	40 (40%)	32(64%)	25(50%)	0.021
Negative symptoms	77 (38.5%)	35(35%)	30(60%)	12(24%)	0.001
Autonomic symptoms	17 (8.5%)	8 (8%)	7(14%)	2(4%)	0.046
Wasting of limbs	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA
Absent ankle jerk	161 (80.5%)	80(80%)	45(90%)	36(72%)	0.075
Impaired pain and temperature	61 (30.5%)	21(21%)	23(46%)	17(34%)	0.006
Impaired vibration and joint position sense	86 (43%)	25(25%)	36(72%)	25(50%)	<0.001

NA = not applicable; CKD = chronic kidney disease.

Table 4: Nerve conduction abnormalities in 200 CKD patients who participated in the study

Nerve conduction parameter	Predialysis patients	Peritoneal dialysis patients	Hemodialysis patients
Median nerve			
Prolonged mdL	15/100 (15%)	9/50 (18%)	4/50 (8%)
Reduced CMAP	30/100 (30%)	41/50 (82%)	16/50 (32%)
Reduced MCV	38/100 (38%)	25/50 (50%)	17/50 (34%)
Ulnar nerve			
Prolonged mdL	12/100 (12%)	7/50 (14%)	5/50 (10%)
Reduced CMAP	30/100 (30%)	19/50 (38%)	20/50 (40%)
Reduced MCV	23/100 (23%)	20/50 (40%)	19/50 (38%)
CP nerve			
Prolonged mdL	15/100 (15%)	23/50 (46%)	13/50 (26%)
Reduced CMAP	65/100 (65%)	35/50 (70%)	39/50 (78%)
Reduced MCV	52/100 (52%)	32/50 (64%)	34/50 (68%)
Posterior tibial nerve			
Prolonged mdL	19/100 (19%)	21/50 (42%)	14/50 (28%)
Reduced CMAP	46/100 (46%)	31/50 (62%)	28/50 (56%)
Reduced MCV	43/100 (43%)	33/50 (66%)	32/50 (64%)
Median nerve (sensory)			
Reduced SNAP	51/100 (51%)	25/50 (50%)	32/50 (64%)
Reduced SCV	66/100 (66%)	26/50 (52%)	28/50 (56%)
Ulnar nerve (sensory)			
Reduced SNAP	62/100 (62%)	29/50 (58%)	32/50 (64%)
Reduced SCV	64/100 (64%)	39/50 (78%)	35/50 (70%)
Sural nerve			
Reduced SNAP	83/100 (83%)	27/50 (54%)	30/50 (60%)
Reduced SCV	51/100 (51%)	40/50 (80%)	44/50 (88%)

mdL = motor distal latency; CMAP = compound muscle action potential; MCV = motor conduction velocity; SNAP = sensory nerve action potential; SCV = sensory conduction velocity; CP = common peroneal; CKD = chronic kidney disease.

was stimulated at the ankle, 80 mm proximal to the recording electrode, lateral to the tendon of tibialis anterior muscle, and below the knee 20–50 mm distal to the proximal part of the caput fibula.

Latency was described as the time from the stimulus to the initial CMAP deflection from the baseline. The CMAP amplitude was measured from the baseline to the negative peak. Conduction velocity was calculated by using the formula - Distance between the proximal and distal stimulation sites / proximal latency- distal latency. The standardized normal adult values of motor nerve conduction studies in both upper and lower extremities as per our electrophysiology lab were shown in Table 1.

The F response also known as the late motor response occurs after the compound muscle action potential.[14] Normal minimal F latency was 25-30 millisec in median and ulnar nerves, while it was 45-59 millisec in common peroneal and posterior tibial nerves.

Sensory conduction studies:

Median and ulnar sensory nerve action potentials (SNAPs) were obtained orthodromically, stimulating from the index finger (median nerve) or the little finger (ulnar nerve) and recording at the wrist. Sural SNAPs were obtained antidromically, recording behind the lateral malleolus and stimulating on the dorsal aspect of the calf, 140 mm proximal to the recording site. The responses were averaged at least 10 times. The standardized normal adult values of sensory nerve conduction studies in both upper and lower extremities as per our electrophysiology lab were shown in Table 2.

Based on electrophysiological parameters, peripheral neuropathy patterns were sub classified into axonal neuropathy, demyelinating neuropathy and mixed neuropathy. In axonal neuropathy, CMAP's decrease, conduction velocities are normal or slightly decreased but never below 75% of the lower limit of normal, distal latencies are normal or slightly prolonged but never greater than 130% of the upper limit of normal. In demyelinating neuropathy, CMAP's are usually normal with marked slowing of conduction velocity (slower than 75% of the lower limit of normal) and/or marked prolongation of distal latency (longer than 130% of the upper limit of normal). It was classified as mixed neuropathy if it has features of both axonal neuropathy and demyelinating neuropathy. Degree of severity of peripheral neuropathy was divided into three groups: normal, early damage and definite damage, according to the number of peripheral nerves involved. Normal or no peripheral damage was defined if nerve conduction studies were normal or only one peripheral nerve was involved. Early damage, if two or three peripheral nerves were involved and definite damage, if more than three peripheral nerves were involved.

Statistical Analysis

The data was collected and tabulated using Microsoft excel 2010 version. Data was analyzed using SPSS version 20. All the continuous variables were expressed as mean ± SD (standard deviation) or median with inter quartile range as appropriate. All categorical variables were expressed as frequencies (percentage). Independent t- test and ANOVA test were applied to compare nominal data between the groups and p value less than 0.05 was considered

Table 5: Comparison of electrophysiological parameters of 200 CKD patients with 25 controls who participated in the study

Electrophysiological parameters	Total patients (n=200)	Predialysis patients (n=100)	Patients in PD group (n = 50)	Patients in HD group (n = 50)	Controls (n = 25)	p value
Median nerve						
dL (milliseconds)	3.8±0.9	3.8±0.8	3.9 ± 1.4	3.7 ± 0.6	3.0 ±0.3	0.001
CV (metres/sec)	49.4±8.0	51.4±4.7	45.3 ± 12.8	49.6 ± 5.2	58.9± 4.1	<0.001
Amplitude (millivolts)	6.6 ±2.6	6.9±2.7	5.8 ± 2.5	6.7 ± 2.5	9.7 ± 2.3	<0.001
F wave :						
Normal	89 (44.5%)	49 (49%)	19 (38%)	21 (42%)	1 (4%)	<0.001
Prolonged	106 (53%)	50 (50%)	28 (56%)	28 (56%)	0 (0%)	
Absent	5 (2.5%)	1 (1%)	3 (6%)	1 (2%)	0 (0%)	
Ulnar nerve						
dL (milliseconds)	2.9±1.5	2.9±2.1	2.9 ± 0.8	2.7 ± 0.5	2.3 ± 0.3	0.141
CV (metres/sec)	51.0 ±6.3	52.3±5.4	49.6 ± 7.1	49.7 ± 6.7	58.6 ±11.8	<0.001
Amplitude (millivolts)	6.6±2.4	6.8±2.2	6.4 ± 3.1	6.3 ± 2.2	8.9 ± 1.5	<0.001
F wave :						
Normal	75 (37.5%)	41 (41%)	16 (32%)	18 (36%)	1 (4%)	<0.001
Prolonged	118 (59%)	56 (56%)	31 (62%)	31 (62%)	0 (0%)	
Absent	7 (3.5%)	3 (3%)	3 (6%)	1 (2%)	0 (0%)	
Common peroneal nerve						
dL (milliseconds)	3.5±1.5	3.5±1.4	3.3 ± 1.9	3.7 ± 1.2	3.7 ± 0.9	0.452
CV (metres/sec)	36.5±15.4	38.7±14.5	31.6 ± 18.3	36.9± 12.9	49.9 ± 3.2	<0.001
Amplitude (millivolts)	2.5±2.3	2.8±2.4	2.3 ± 2.4	2.2 ± 1.9	7.2 ± 2.4	<0.001
F wave :						
Normal	107(53.5%)	60 (60%)	18 (36%)	29 (58%)	1 (4%)	<0.001
Prolonged	10 (5%)	3 (3%)	1 (2%)	6 (12%)	0 (0%)	
Absent	82 (41%)	37 (37%)	31 (62%)	14 (28%)	0 (0%)	
Posterior tibial nerve						
dL (milliseconds)	3.6±1.6	3.7±1.4	3.1 ± 1.9	3.9 ± 1.3	3.4 ± 0.4	0.038
CV (metres/sec)	36.7±14.6	39.2±12.9	30.8 ± 18.3	37.4± 11.7	49.5 ± 3.2	<0.001
Amplitude (millivolts)	5.0±4.2	5.9±4.5	3.4 ± 3.3	4.9 ± 3.8	11.1 ± 3.1	<0.001
F wave :						
Normal	107 (53.5%)	58 (58%)	23 (46%)	26 (52%)	1 (4%)	<0.001
Prolonged	39 (19.5%)	20 (20%)	4 (8%)	15 (30%)	0 (0%)	
Absent	54 (27%)	22 (22%)	23 (46%)	9 (18%)	0 (0%)	
Median nerve sensory						
dL (milliseconds)	2.6±0.9	2.7±0.9	2.3 ± 1.2	2.8 ± 0.7	2.5 ± 0.2	0.020
CV (metres/sec)	42.9±14.7	43.7±13.3	39.7 ± 19.6	44.4± 11.2	55.8± 5.0	<0.001
Amplitude (millivolts)	11.9±10.4	11.4±9.1	12.9 ± 13.1	11.9± 10.0	26.8±9.1	<0.001
Ulnar nerve sensory						
dL (milliseconds)	2.0 ±0.9	1.9 ±0.9	1.8 ± 1.0	2.2 ± 0.7	2.0 ± 0.2	0.23
CV (metres/sec)	39.8±18.9	39.2±19.7	37.8 ± 21.2	43.1± 14.2	57.5 ± 4.9	<0.001
Amplitude (millivolts)	7.4±7.0	7.8±7.4	6.6 ± 6.2	7.6 ± 6.9	16.7 ± 8.9	<0.001
Sural nerve sensory						
dL (milliseconds)	1.7±1.4	1.6±1.4	1.4 ± 1.4	2.1 ± 1.4	2.5 ± 0.2	0.002
CV (metres/sec)	29.4±24.1	29.4±24.5	25.9 ± 25.5	32.9± 21.8	53.9 ± 3.8	<0.001
Amplitude (millivolts)	5.0±6.5	5.4±6.9	5.2 ± 7.3	4.1 ±4.7	19.3 ± 9.1	<0.001

dL = distal latency; CV = conduction velocity; PD = peritoneal dialysis; HD = hemodialysis

statistically significant.

Results

Between May 2015 and December 2016, 200 consecutive patients with chronic kidney disease who consented to participate were included in the study. These 200 patients were divided into three groups – predialysis group, hemodialysis group and peritoneal dialysis group.

Prevalence of peripheral neuropathy in chronic kidney disease

Prevalence of peripheral neuropathy in chronic kidney disease in the present study was 50% based on clinical symptoms and 89% based on electrophysiological parameters. Among 200 patients in the present study, peripheral neuropathy was present in 178 patients.

Demographic characteristics of chronic kidney disease patients

Mean age of 200 CKD patients who participated in the study was 54.1 ± 11.9 years.135 (67.5%) patients were male and 65 (32.5%) patients were female. Mean duration of disease in 200 patients of CKD was 4.2 ± 3.7 years. Mean age of 25 controls who participated in the study was 33.4 ± 10.9 years.10 (40%) were male and 15 (60%) were female.

102 patients (51%) belonged to rural areas, while 98 patients (49%) belonged to urban areas.

Symptoms and signs of peripheral neuropathy in chronic kidney disease

Positive sensory symptoms were seen in 97(48.5%) patients, while negative sensory symptoms were seen in 77(38.5%) patients. Autonomic symptoms were seen in 17(8.5%) patients. 161(80.5%) patients had absent ankle jerk. Impaired pain and temperature sensation was noted in 61(30.5%) patients, while impaired vibration and joint position sense was noted in 86(43%) patients. Motor weakness was noted in 6(3%) patients.

Comparison of symptoms and signs of patients in predialysis group, peritoneal dialysis group and hemodialysis group is shown in Table 3.

On comparing symptoms and signs of 200 CKD patients, patients in peritoneal dialysis group showed statistical significance in presence of motor weakness ($p<0.001$), positive symptoms ($p=0.021$), negative symptoms ($p=0.001$), autonomic symptoms ($p= 0.046$), impaired pain and temperature sensation ($p=0.006$) and impaired vibration and joint position sense ($p <0.001$).

Meanserum creatinine of 200 CKD patients who participated in the study was 6.4 ± 3 mg/dl. Mean serum urea of 200 CKD patients who participated in the study was 97.6 ± 43.8 mg/dl.

On the basis of electrophysiological study, peripheral neuropathy was found in 178 patients. Distal motor latencies, compound muscle action potential (CMAP) and motor conduction velocity abnormalities of right median nerve were present in 14%, 46.5% and 33.5% respectively. Distal motor latencies, CMAP and motor conduction velocity abnormalities of right ulnar nerve were present in 12%, 34.5% and 31%

respectively. Distal motor latencies, CMAP and motor conduction velocity abnormalities of common peroneal nerve were present in 25.5%, 69.5% and 59% respectively. Distal motor latencies, CMAP and motor conduction velocity abnormalities of posterior tibial nerve were present in 27%, 53.5% and 54% respectively. Sensory conduction velocity and sensory nerve amplitude (SNAP) abnormalities of right median nerve were present in 61.5% and 52.5% respectively. Sensory conduction velocity and SNAP abnormalities of right ulnar nerve were present in 62.5% and 68% respectively. Sensory conduction velocity and SNAP abnormalities of sural nerve were present in 54% and 83.5% respectively.

Nerve conduction abnormalities in CKD patients in relation with stage of the disease is shown in Table 4.

Comparison of electrophysiological parameters of 200 chronic kidney disease patients

Comparison of electrophysiological parameters of 200 CKD patients with 25 controls who participated in the study is shown in Table 5.

On comparing electrophysiological data of 100 predialysis patients, 50 peritoneal dialysis patients, 50 hemodialysis patients and 25 controls, patients in peritoneal dialysis group showed statistical significance in presence of prolonged median nerve motor distal latency (p = 0.001), low median nerve motor conduction velocity (p <0.001), low median nerve motor amplitude (p <0.001), prolonged median nerve F wave (p <0.001), low ulnar nerve motor conduction velocity (p <0.001), prolonged / absent ulnar F wave (p <0.001), low common peroneal nerve motor conduction velocity (p <0.001), absent common peroneal F wave (p <0.001), low posterior tibial nerve motor conduction velocity (p <0.001), low posterior tibial nerve motor amplitude (p <0.001),absent posterior tibial nerve F wave (p <0.001), low median nerve sensory conduction velocity (p <0.001), low ulnar nerve sensory conduction velocity (p <0.001), low ulnar nerve sensory amplitude (p <0.001)and low sural nerve sensory conduction velocity (p <0.001).

Patients on hemodialysis showed statistically significant low ulnar nerve motor amplitude (p <0.001), low common peroneal nerve motor amplitude (p <0.001), prolonged posterior tibial nerve motor distal latency (p = 0.038), prolonged median nerve sensory distal latency (p = 0.020), prolonged sural nerve sensory distal latency (p = 0.002) and low sural nerve sensory amplitude (p <0.001).

Patients in predialysis group showed statistically significant low median nerve sensory amplitude (p <0.001).

Severity of peripheral neuropathy in 200 chronic kidney disease patients

Definite damage was seen in 133 patients (66.5%), early damage was seen in 45 patients (22.5%) while 22 patients (11%) had no significant peripheral neuropathy. In predialysis patients (n=100); 63 patients (63%) had definite damage and 24 patients (24%) had early damage. In peritoneal dialysis patients (n=50); 34 patients (68%) had definite damage and 8 patients (16%) had early damage. In hemodialysis patients (n=50); 36 patients (72%) had definite damage and 13 patients (26%) had early damage. No significant neuropathy was seen in 13 patients (13%) of predialysis group, 8 patients (16%) of peritoneal dialysis group and 1 patient (2%) of hemodialysis group. There was no statistically significant difference in the patterns of peripheral neuropathy in urban and rural patients.

Discussion

Chronic kidney disease is characterized by multiple neurological complications, of which uremic neuropathy has been recognized as most common complication, resulting in significant morbidity. The present study was undertaken to study the prevalence, clinical and electrophysiological features of peripheral neuropathy in CKD patients with respect to severity of disease and mode of dialysis. Nerve conduction studies are most commonly used non-invasive procedure used for establishing presence of peripheral nervous system involvement and type of involvement. The present study showed a high prevalence of uremic neuropathy. 89% of CKD patients had electrophysiological evidence of peripheral neuropathy, of which only 50% were symptomatic. 39% of CKD patients had asymptomatic peripheral neuropathy, which was more common in predialysis group. Symptomatic peripheral neuropathy was more common in peritoneal dialysis group. This further strengthens the need for regular nerve conduction studies for early diagnosis and appropriate management of peripheral neuropathy. Prevalence of peripheral neuropathy in uremia in the present study was slightly higher when compared to other published studies[16,17] like Lobna et al (62.5%) and Madhusudhana et al (65%), probably due to inclusion of more number of patients on dialysis in the present study. According to Hari et al[18] from North India, peripheral neuropathy was present in 70% of predialysis patients, which was 87% in the present study. Another study from North India by Vinod et al,[19] prevalence of polyneuropathy was 75.26% and mononeuropathy was 6.51%. Prevalence of peripheral neuropathy in patients on hemodialysis and peritoneal dialysis based on electrophysiological studies were 98% and 84% respectively in the present study. According to Tilki et al,[20] peripheral neuropathy was seen in 97.6% of chronic kidney disease patients on hemodialysis, which was 86.8% according to Janda K et al[21]and 60% according to Bolton et al.[22] 77.4% of chronic kidney disease patients on peritoneal dialysis showed evidence of peripheral neuropathy according to Janda K et al.[21] Prevalence of peripheral neuropathy in dialysis patients was slightly higher in the present study when compared to other published international studies. But however literature on peripheral neuropathy in dialysis patients is sparse in Indian literature, especially in South India, where there are few endemic areas of CKD.

Positive sensory symptoms (64%) and negative sensory symptoms (60%) were more common in peritoneal dialysis patients when compared with other groups. Autonomic symptoms were seen in 17(8.5%) patients, which were more common in peritoneal dialysis patients. Motor weakness (p<0.001), positive symptoms (p=0.021), negative symptoms (p=0.001), autonomic symptoms (p= 0.046), impaired pain and temperature sensation (p=0.006) and impaired vibration and joint position sense (p <0.001) were more common peritoneal dialysis patients, when compared to other groups. Symptomatic neuropathy was seen in 51% of predialysis chronic kidney disease patients according to Hari et al,[18] which was comparable to the

Table 6 : Comparison of electrophysiological parameters in peritoneal and hemodialysis patients as reported in published studies

Electrophysiological parameters	Sultan[16]	Khadija[18]	Present study	Tilki[19]	Donald[20]	Present study	Deniz[21]	Sultan[16]	T Ogura[22]	Present study
	Predialysis patients			Peritoneal dialysis patients			Hemodialysis patients			
Country	Egypt	Pakistan	India	Turkey	Canada	India	Turkey	Egypt	Japan	India
Sample size	20	30	100	12	29	50	38	20	70	50
Electrophysiological parameters										
Median nerve										
dL (milliseconds)	3.1 ± 0.6	8.3 ± 0.2	3.8±0.8	0.85±0.71	NA	3.9 ± 1.4	3.9±0.6	4.2 ± 1.1	3.7 ± 0.3	3.7 ± 0.6
CV (metres/sec)	55.6 ± 6.8	53.7 ± 2.2	51.4±4.7	40.39±1.47	48.6±5.5	45.3 ± 12.8	54.2±4.5	51.1 ± 3.9	52.1 ± 3.8	49.6 ± 5.2
Amplitude (millivolts)	12.7 ± 5.5	13.2 ± 0.4	6.9±2.7	5.53±0.99	NA	5.8 ± 2.5	7.0±3.2	9.6 ± 3.3	NA	6.7 ± 2.5
Ulnar nerve										
dL (milliseconds)	2.6 ± 0.5	NA	2.9±2.1	0.2±0.9	NA	2.9 ± 0.8	NA	2.7 ± 0.5	NA	2.7 ± 0.5
CV (metres/sec)	57.7 ± 6.5	NA	52.3±5.4	28.6 ±1.3	46.9±5.9	49.6 ± 7.1	57.0 ± 4.9	56.9 ± 6.1	NA	49.7 ± 6.7
Amplitude (millivolts)	13.8 ± 3.5	NA	6.8±2.2	1.2±0.8	NA	6.4 ± 3.1	8.3 ± 2.2	13.8 ± 3.4	NA	6.3 ± 2.2
Common peroneal nerve										
dL (milliseconds)	5.4 ± 1.3	9.4 ± 0.1	3.5±1.4	0.7±1.1	NA	3.3 ± 1.9	NA	5.4 ± 1.0	NA	3.7 ± 1.2
CV (metres/sec)	43.5 ± 4.2	56.3 ± 1.7	38.7±14.5	66.7±1.0	38.7±3.9	31.6 ± 18.3	40.8±7.2	43.6 ± 4.9	NA	36.9± 12.9
Amplitude (millivolts)	3.8 ± 2.5	4.5 ± 1.1	2.8±2.4	1.4±0.8	NA	2.3 ± 2.4	3.2±2.0	3.6 ± 2.5	NA	2.2 ± 1.9
Posterior tibial nerve										
dL (milliseconds)	5.1 ± 1.0	NA	3.7±1.4	0.2±1.1	NA	3.1 ± 1.9	NA	5.3 ± 1.2	5.3 ± 0.9	3.9 ± 1.3
CV (metres/sec)	42.9 ± 5.4	NA	39.2±12.9	51.2±1.3	NA	30.8 ± 18.3	37.3±4.2	42.6 ± 4.4	41.6 ± 5.1	37.4± 11.7
Amplitude (millivolts)	12.4 ± 5.0	NA	5.9±4.5	1.9±1.1	NA	3.4 ± 3.3	5.7±2.5	11.3 ± 6.0	NA	4.9 ± 3.8
Median nerve sensory										
dL (milliseconds)	NA	NA	2.7±0.9	1.5±1.1	NA	2.3 ± 1.2	NA	NA	NA	2.8 ± 0.7
CV (metres/sec)	NA	NA	43.7±13.3	27.3±3.8	38.3±9.0	39.7 ± 19.6	52.1±5.5	NA	50.9 ± 5.0	44.4± 11.2
Amplitude (millivolts)	NA	NA	11.4±9.1	6.8±5.4	NA	12.9 ± 13.1	NA	NA	NA	11.9± 10.0
Ulnar nerve sensory										
dL (milliseconds)	2.9 ± 0.3	NA	1.9 ±0.9	0.8±0.6	NA	1.8 ± 1.0	NA	2.90 ±0.30	NA	2.2 ± 0.7
CV (metres/sec)	54.5 ± 5.4	NA	39.2±19.7	6.1±0.9	38.4±4.5	37.8 ± 21.2	52.6±4.8	54.65 ± 5.42	NA	43.1± 14.2
Amplitude (millivolts)	14.0 ± 16.3	NA	7.8±7.4	0.9 ±3.8	NA	6.6 ± 6.2	NA	51.78 ± 18.0	NA	7.6 ± 6.9
Sural nerve sensory										
dL (milliseconds)	3.9 ± 0.8	NA	1.6±1.4	NA	NA	1.4 ± 1.4	NA	3.93 ± 0.6	NA	2.1 ± 1.4
CV (metres/sec)	39.9 ± 5.4	NA	29.4±24.5	17.1±0.7	NA	25.9 ± 25.5	32.5±18.7	40.1 ± 5.92	44.7 ± 5.0	32.9± 21.8
Amplitude (millivolts)	9.8 ±n 3.8	NA	5.4±6.9	4.9 ±3.9	NA	5.2 ± 7.3	NA	10.67 ± 4.64	NA	4.1 ±4.7

dL = distal latency ; CV = conduction velocity; NA = not applicable.

present study. According to Krishnan et al[23] and Laaksonen et al,[8] symptomatic peripheral neuropathy was seen in 91% and 62% of chronic kidney disease patients respectively.

Electrophysiological parameters in chronic kidney disease

Most common nerves involved in the present study were sural nerve, ulnar sensory nerve, median sensory nerve followed by common peroneal nerve and posterior tibial nerve in all groups. Lower limbs were most commonly affected than upper limbs, which indicate a length dependent pattern of peripheral neuropathy. Sensory nerves were commonly affected than motor nerves in the present study. According to Hari et al,[18] mean nerve conduction velocities (m/sec) of right median, ulnar, common peroneal and posterior tibial nerves were 51.34±6.07, 53.04±5.91, 44.72±6.14 and 44.2±5.17 respectively in predialysis patients, which were almost similar to the present study.

Comparison of electrophysiological parameters in 100 patients of predialysis group with other published international studies[16,24] is shown in Table 6. Indian data regarding electrophysiological parameters in predialysis patients is sparse.

On comparing electrophysiological parameters of predialysis patients, motor distal latency and motor conduction velocity were similar to other published studies but motor amplitudes were low in the present study. In predialysis patients (n=100); mononeuropathy was seen in 3 patients in form of carpal tunnel syndrome. 87% patients had significant peripheral neuropathy in patients of predialysis group.

Comparison of electrophysiological profile in 50 patients of peritoneal dialysis group with other published international studies[20,25] is shown in Table 6.Indian data regarding electrophysiological parameters in peritoneal dialysis patients is sparse.

On comparing electrophysiological parameters of patients in peritoneal dialysis group with other published studies, motor amplitude and motor conduction velocity were higher when compared to other published studies. In peritoneal dialysis patients (n=50); 4 patients had carpal tunnel syndrome. 84% patients had significant peripheral neuropathy in patients of peritoneal dialysis group.

Comparision of electrophysiological profile in 50 patients of hemodialysis group with other published international studies[16,26,27] is shown in Table 6. Indian data regarding electrophysiological parameters in hemodialysis patients is sparse.

On comparing electrophysiological parameters of hemodialysis patients with other published studies, common peroneal nerve motor amplitudes, posterior tibial nerve motor amplitudes, ulnar nerve sensory amplitudes and sural nerve sensory amplitudes were lower in the present study probably due

to presence of edema. In hemodialysis patients (n=50); 5 patients had mononeuropathy. 98% patients had significant peripheral neuropathy in patients of hemodialysis group.

The most common patterns of peripheral neuropathy in 100 patients of predialysis group were pure axonal sensorimotor neuropathy pattern (33%) followed by mixed sensorimotor neuropathy pattern (30%). The most common patterns of peripheral neuropathy in 50 patients of peritoneal dialysis group were pure axonal sensorimotor neuropathy pattern (44%) and mixed sensorimotor neuropathy pattern (34%). The most common patterns of peripheral neuropathy in 50 patients of hemodialysis group were mixed sensorimotor axonal neuropathy pattern (42%) followed by pure axonal sensorimotor neuropathy pattern (18%).

Limitations of the present study

1. This study is a hospital based study, so it is not an accurate measure of community based prevalence of neuropathy in CKD patients.
2. Electrophysiologic parameters might be slightly altered due to presence of edema in CKD patients.

Conclusion

Peripheral neuropathy is common in chronic kidney disease with highest prevalence in hemodialysis group electrophysiologically with almost similar prevalence in peritoneal dialysis and predialysis patients. However symptomatic peripheral neuropathy is more common in peritoneal dialysis group. Severity of peripheral neuropathy is also more in hemodialysis patients than peritoneal dialysis patients. Severity of peripheral neuropathy increases as uremia worsens. Newer treatment modalities are required to manage uremic neuropathy in early stage.

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