ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 09 | September - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ASSOCIATION OF PERIPHERAL NEUROPATHY IN CHRONIC KIDNEY DISEASE- A CLINICO-DEMOGRAPHICAL STUDY

Neurology

Arvind Kankane	DM Neurology Professor and Head, Department of Neurology, M.L.B. Medical College, Jhansi, Uttar Pradesh.
Dr A K Pandey	DM Neurology Assistant Professor Department of Neurology, M.L.B. Medical College, Jhansi, Uttar Pradesh.
Manish Ramesh Patil	DM Neurology Assistant Professor, Department of Neurology, M.L.B. Medical College, Jhansi, Uttar Pradesh
Shailja Singh	Junior Resident, Department of Medicine, M.L.B. Medical College, Jhansi, Uttar Pradesh
Arpit Agarwal	DM Neurology Senior Resident, Department of Neurology, M.L.B. Medical College, Jhansi, Uttar Pradesh

ABSTRACT

Introduction Approximately 60% of the population with CKD will encounter neurological complications. Uremic neuropathy is one of the most common neurological complications of uremia. Distal symmetrical sensorimotor peripheral neuropathy is the most common pattern of neuropathy in CKD, and it predominantly affects lower limbs when compared to upper limbs. **Aims and Objective** To determine prevalence and type of neuropathy in CKD patients with their clinic-demographic profile. To evaluate MNSI score as tool to asses peripheral neuropathy in CKD. **Methodology** 100 patients of diagnosed CKD were enrolled following the inclusion and exclusion criteria and were assessed for peripheral neuropathy both clinically and electrophysiologically. **Results** Among CKD patients men were more affected with PN than women. With increasing duration of uremia the prevelance of neuropathy increased most in the group of 2-3 years. Most common form of neuropathy was distal symmetrical axonal sensory motor neuropathy. 65 % cases were having neuropathy. Patients on HD had higher percentage of neuropathy than not on HD. MNSI score was found to be statistically significant among all CKD groups. **Conclusion** Peripheral neuropathy is very commonly associated with CKD , more common in dialysis patients as compared to pre dialysis patients. Males are affected more than female. MNSI score is good tool to asses neuropathy in patients of CKD

KEYWORDS

INTRODUCTION

Chronic kidney disease(1,2) (CKD) is defined as the kidney damage lasting more than 3 months, which is characterized by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate.

Approximately 60% of the population with CKD will encounter neurological complications(3), which affects at all levels of nervous system, peripheral and central, resulting in altered mental state, continued disability and weakness.(4) Uremic neuropathy is one of the most common neurological complications of uremia. Distal symmetrical sensorimotor peripheral neuropathy is the most common pattern of neuropathy in CKD, and it predominantly affects lower limbs when compared to upper limbs.

Uremic neuropathy usually involves large diameter axons.(5) Uremic neuropathy is often multifactorial, which is exacerbated by nutritional deficiency, hypocalcemia, and hypomagnesemia. Uremic toxins such as guanidine compounds, polyamines, phenol metabolites, myoinositol, and 3-carboxy-4-methyl-5-propyl-2-fluranpropanoic acid were proposed as causative agents of uremic neuropathy.(6)

Chronic kidney disease (CKD) is associated with decreased functional independence, (7) falls,(8) frailty(9) leading to poor quality of life and accelerated aging [6]. Sensory and proprioceptive inputs to the central nervous system and appropriate motor outputs to the skeletal muscle are imperative to maintain balance and walking ability(10).

Abnormal gait, falls, and fractures are common in patients with CKD and in clinical practice it is noted that neuropathy increases the presence of all these outcomes(11). In advanced CKD, as well as in patients who are dialysis dependent or end stage kidney disease, uremic neuropathy has been determined to be a progressive sensorimotor axonal neuropathy(12).

Even though peripheral neuropathy is a well-described neurological complication in end-stage renal disease patients, there are no major central Indian studies addressing this issue. The present study was done to assess the prevalence and clinical and electrophysiological features of peripheral neuropathy patients of CKD (both on Dialysis and pre Dialysis)

AIMS AND OBJECTIVES:

- To determine the prevalence and type of peripheral neuropathy in patients with chronic kidney disease
- The clinico-demographic profile of CKD patients having peripheral neuropathy in relation to uremia duration and creatinine stage in CKD both, on hemodialysis & not on hemodialysis.
- To evaluate MSNI score as a tool for assessing peripheral neuropathy in CKD patients

MATERIALS AND METHODS:

Patients –

It was a cross-sectional study conducted in 100 CKD patients attending the Hemodialysis unit , OPD, inpatient in department of Medicine and Neurology, Maharani Laxmi Bai Medical College, Jhansi up, between April 2022 to April 2023 and assessed for peripheral neuropathy. Ethics committee approval was duly taken with the study conducted in accordance with the guidelines. Informed consent was taken from each participant.

Inclusion and Exclusion Criteria-

- All patients irrespective of age and sex with the CKD.
- eGFR <60ml/min/1.73m2 determined by the MDRD formula (186.3* creatinine in mg/dl) - 1.154*(Age)-0.203 * (.742)(if female).
- Ultrasound abdomen evidence of CKD (increased renal echogenicity, reduced renal cortical thickness, reduced renal length <9cm.)

Patient denying consent or patient who had renal transplant and on peritoneal dialysis. Patient with other known cause of peripheral neuropathy such as hypothyroidism,diabetes mellitus, tuberculosis and Hansen's disease. Patients on drug having neuropathy as established toxicity, malignancy,vit.B12 deficiency were excluded.

METHODOLOGY-

They were subjected to detailed history, general-physical examination, and neurological examination and were asked detailed history regarding the duration of neurological symptoms, whether the patient is already on any renal replacement therapy, if the patient is already on hemodialysis then the duration of his hemodialysis period was

recorded.. History regarding any previous/concomitant illness intake of drugs, prescription as well as recreational, were elicited and recorded when deemed relevant. The patients were asked to answer questions from MNSI questionnaire. Then physical assessment according to MNSI physical assessment chart was carried out and points filled. Their routine renal and other biochemical investigations including blood urea (mg/dL), serum creatinine (mg/dL), serum corrected calcium levels (mg/dL), serum phosphorous levels (mg/dL), calcium phosphate product, serum protein (g/dL), iPTH levels (pg/mL), vitamin B12 levels(pg/mL), serum sodium (meq/L), serum potassium (meq/L), blood sugar were carried out as per the standard methods used in the Department of Biochemistry, MLC MC, Jhansi, while eGFR was estimated using MDRD equation. Each patient was also subjected to nerve conduction studies (NCS) to determine motor nerve conduction velocities (NCVs) of median, ulnar, peroneal, and tibial nerves unilaterally (right). Patients continued receiving anti-hypertensives, diuretics, iron, and calcium supplements as per their renal and biochemical profiles.

Nerve Conduction Studies

All cases were subjected to NCSs 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.

Motor Nerve Conduction Studies Procedure

The gain was normally set at 2–5 mV per division for the motor conduction studies.[14] 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 ms for the motor NCSs. To achieve supramaximal stimulation, current in the range of 20–50 mA was used. The underlying nerve fibers were brought to action potential as the current was steadily increased from a baseline, usually by 5–10 mA. 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, the CMAP will 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 inter-phalangeal joint. Mid arm, ante-cubital 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. 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 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 using the formula as follows: Distance between the proximal and distal stimulation sites/proximal latency − distal latency.

The F response also known as the late motor response occurs after the CMAP. [16] Normal minimal F latency was 25–30 ms in median and ulnar nerves, while it was 45–59 ms 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.

Based on electrophysiological parameters, peripheral neuropathy patterns were subclassified into axonal neuropathy, demyelinating neuropathy, and mixed neuropathy. In axonal neuropathy, CMAPs decrease, conduction velocities are normal or slightly decreased but never <75% of the lower limit of normal, and distal latencies are normal or slightly prolonged but never >130% of the upper limit of normal. In demyelinating neuropathy, CMAPs 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

RESULTS

Demographic characteristics and clinical Signs

Out of 100 subjects 62 were males, 38 were females. Males were affected more (67.74%), than females (60.52%) (Table-1). Most common sign observed is absent ankle reflex (41.06%), followed by abnormal monofilament test (32.37%), absent vibration perception (23.31%), ulcerations (6.68%).(Fig-1)

Distribution of Neuropathy

Out of 56 HD patients, 43 (76.78%) patients and out of 44 pre-HD patients, 22(50 %) showed peripheral neuropathy (Fig-3). Age group of >60 years showed maximum percentage of peripheral neuropathy (93.11%), followed by 30-60 years (59.57%), absent in <30 years. On classifying neuropathy according to duration of uremia, it was seen that is was maximum in duration between 2 to 3 years (92.31%), followed by >3 years (85.71%), 1-2 years (45.71%)(Table-2). Patients with creatinine value >8.9mg/dl (100%) had maximum percentage of neuropathy .

The mean serum creatinine of patients was 5.84 ± 2.05 mg/dl .The prevalence of clinical peripheral neuropathy in the present study was 65%. The most common pattern of neuropathy is mixed sensory motor (Axonal + demyelination) in pre -HD patients (82.60%), HD patients (97.76%). Pure Axonal sensory motor pattern seen in pre-HD patients (17.39%), HD patients (2.38%) (Fig-2).

In our study of 100 patients which includes CKD patients from stage III to stage V with or without on hemodialysis. The smallest score obtained was 2 and the largest score obtained was 7 with a mean score of 2.580±2.069. Further breaking down 3 patient from CKD stage III had scored >3 in MNSI, 23 patients has scored >3 in MNSI. Finally among the CKD Stage V patients, 72 patients have scored >3 in MNSI. D The distribution of MNSI scores among different CKD subtype was statistically significant ($p<0.005$) (Table-3)(fig-4)

It is observed in our study that with increasing creatinine level the percentage of neuropathy increases. As seen in below (Fig-5) the group with above 5 mg creatinine have the highest percentage of neuropathy and the association is statistically significant.($p<0.05$)

Table 1: Gender And UPN Distribution

Gender	UPN		Total
	Present	Absent	
Male	42	20	62
Female	23	15	38
Total	65	35	100

Table 2: Duration Of Uraemia

Duration of uraemia	Neuropathy present	Total
<1 year	1 (8.3%)	12
1-3 years	16 (45.71%)	35
2-3 years	36 (92.31%)	39
>3 years	12 (85.71%)	14

Table 3: MNSI Scores And CKD Stages

MNSI Scores	CKD Stages			Total
	III	IV	V	
1.5-2.5	00	00	02	02
3-5.5	01	09	48	58
6-10	00	00	06	06
>10	02	14	18	34
Total	03	23	74	100

DISCUSSION:

Among the myriad complications manifesting in ESRD, polyneuropathy has been recognized as the most common complication. Uremic neuropathy presents as distal painless, progressive, symmetrical, sensorimotor polyneuropathy; as the neuropathy worsens the symptoms including dysesthesia manifest and ascend. There is segmental demyelination and axonal degeneration in peripheral nerves. Peripheral neuropathy complicating CKD was described as early as 1962 by Arthur K. Asbury.(13)

In this study, males (67.74%) more than females (60.52%) were affected. In a study by Jedras M et al (14) and Madhusudan et al(17) the number of male patients having neuropathy were more than that of female patients.

In this study maximum neuropathy seen with age group >60 years (94.11%) , followed by 30-60 years (68.57%), absent in <30 years . Different studies have shown diiferent results as of Alagesan et al(15) and Madhusudan et al (17) study showed neuropathy to be most in in 35-44 age group (27.8%) while Sultan LI et al(16), study showed maximum neuropathy >50 year age group (84.62%). The difference in age groups might be due to presence of more severe disease in the the respective groups.

In this study neuropathy is maximum when duration of uremia between 2 to 3 years (84.61%), followed by >3 years (78.57%), 1-2 years (42.85%). Alagesan et al(15), study showed 19.8% neuropathy in <3 years and 45.41% had neuropathy >3 years of uraemia. Madhusudan et al,(17) in his study found that prevalence increases with long duration of symptom. In our study out of 100 CKD patients 65 (65%) patients had evidence of peripheral neuropathy, which is comparable with Dushyant babu jasti et al(18)89%, Hari et(12) 70%, and Tilki et al(19) 97.6% neuropathy.

The distribution of MNSI scores among different CKD subtype was statistically significant (χ^2=18.3173,p<0/05). Our study reiterates the fact that MNSI could serve as a valid test to diagnose Uremic neuropathy with the view that early management may have a positive impact on the quality of life of the patient.

It was observed that with increasing creatinine level the prevalence of peripheral neuropathy increased. H K Aggarwal et al(12), in their study on 100 patients found that prevalence of peripheral neuropathy increased with a raise in serum creatinine, This observation was confirmed in other studies as well [(19–21)] .

CONCLUSION

Peripheral neuropathy is very commonly associated with CKD , more common in dialysis patients as compared to pre dialysis patients. Although the exact patho-physiological mechanism leading to this now common entity is not completely understood, despite extensive on-going research, it is imperative that every treating physician has in-depth knowledge regarding this disease process. In dialysis patient the most common form of neuropathy was found to be mixed axonal sensory motor neuropathy. It increases with duration and severity of CKD. Distal symmetrical mixed sensory motor polyneuropathy is more common in lower limb than upper limb. CKD and leads to a decreased sense of wellbeing. Hence, along with prevention and management of life-threatening complication of CKD, early detection of peripheral neuropathy must be a priority among physicians and nephrologists alike, who deal with patients of CKD on day to day basis. Our study reiterates the fact that MNSI could serve as a valid test to diagnose Uremic neuropathy with the view that early management may have a positive impact on the quality of life of the patient.

NCV is a simple and inexpensive tool to detect peripheral neuropathy very early in CKD patients. It can be easily and frequently used in our country where there is monetary shortage, and provide in depth knowledge of the condition. This will further help in directing funds in proper care and management of CKD patients and their other life threatening complication. The patients with undetermined neuropathy should be screened for kidney function test as a routine.

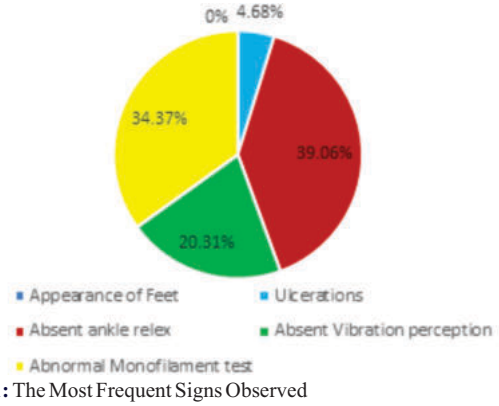

Fig-1: The Most Frequent Signs Observed

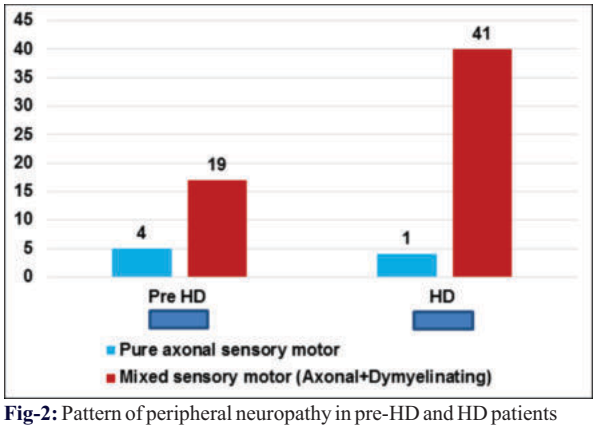

Fig-2: Pattern of peripheral neuropathy in pre-HD and HD patients

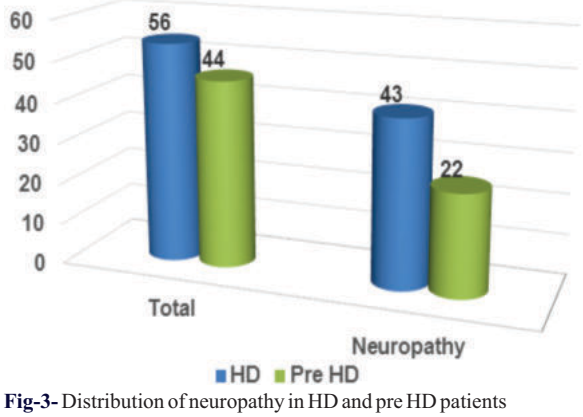

Fig-3- Distribution of neuropathy in HD and pre HD patients

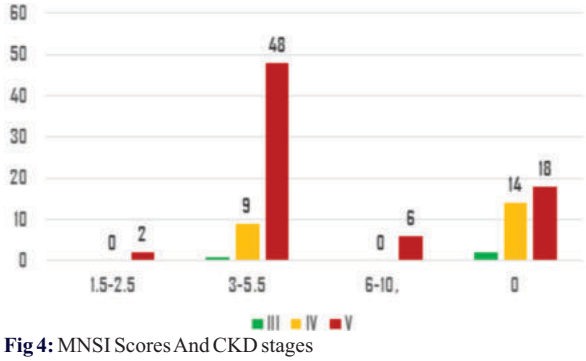

Fig 4: MNSI Scores And CKD stages

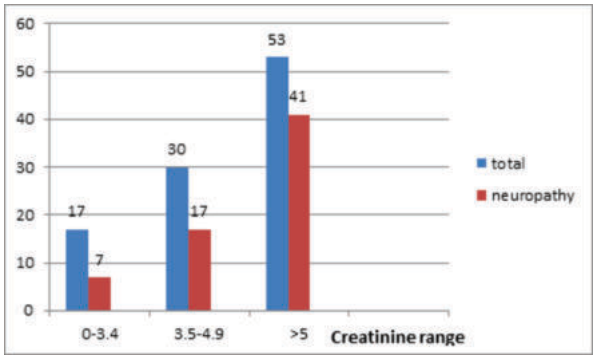

Fig-5 Distribution of Neuropathy according to serum creatinine

REFERENCES

1. Foundation NK. KDOQI clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease. American journal of kidney diseases: the official journal of the National Kidney Foundation. 2006;47(5 Suppl 3):S11–145.
2. Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: systematic review. BMC public health. 2008;8(1):1–13.
3. Brouns R, De Deyn PP. Neurological complications in renal failure: a review. Clinical neurology and neurosurgery. 2004;107(1):1–16.
4. Krishnan AV, Kiernan MC. Neurological complications of chronic kidney disease. Nature Reviews Neurology. 2009;5(10):542–51.
5. Nielsen VK. The peripheral nerve function in chronic renal failure: II. Intercorrelation of clinical symptoms and signs and clinical grading of neuropathy. Acta Medica Scandinavica. 1971;190(1–6):113–7.
6. Halar EM, Brozovich FV, Milutinovic J, Inouye VL, Becker VM. H-reflex latency in uremic neuropathy: correlation with NCV and clinical findings. Archives of Physical Medicine and Rehabilitation. 1979;60(4):174–7.
7. Smyth A, Glynn LG, Murphy AW, Mulqueen J, Canavan M, Reddan DN, et al. Mild chronic kidney disease and functional impairment in community-dwelling older adults. Age and ageing. 2013;42(4):488–94.
8. Bowling CB, Hall RK, Khakharia A, Franch HA, Plantinga LC. Serious fall injury history and adverse health outcomes after initiating hemodialysis among older US adults. The Journals of Gerontology: Series A. 2018;73(9):1216–21.
9. Walker SR, Brar R, Eng F, Komenda P, Rigatto C, Prasad B, et al. Frailty and physical function in chronic kidney disease: the CanFIT study. Canadian journal of kidney health and disease. 2015;2:67.
10. Kooman JP, Kotanko P, Schols AM, Shiels PG, Stenvinkel P. Chronic kidney disease and premature ageing. Nature Reviews Nephrology. 2014;10(12):732–42.
11. Arnold R, Issar T, Krishnan AV, Pussell BA. Neurological complications in chronic kidney disease. JRSM cardiovascular disease. 2016;5:2048004016677687.
12. Aggarwal HK, Sood S, Jain D, Kaverappa V, Yadav S. Evaluation of spectrum of peripheral neuropathy in predialysis patients with chronic kidney disease. Renal failure. 2013;35(10):1323–9.
13. ASBURY: Uremic polyneuropathy - Google Scholar [Internet]. [cited 2023 May 31]. Available from: https://scholar.google.com/scholar_lookup?hl=en&volume=8&publication_year=1963&pages=413-428&journal=%00null%00&issue=%00null%00&issn=%00null%00&author=AK+Asbury&author=M+Victor&author=RD+Adams&title=Uremic+polyneuropathy&pmid=%00empty%00&doi=%00empty%00#d=gs_cit&t=1685520227791&u=%2Fscholar%3Fq%3Dinfo%3AKKBA-JICg0wJ%3Ascholar.google.com%2F%26 output%3Dcite%26scirp%3D0%26hl%3Den
14. Jedras M, Zakrzewska-Pniewska B, Wardyn K, Switalski M. Uremic neuropathy–I. Is uremic neuropathy related to patient age, duration of nephropathy and dialysis treatment? Polskie archiwum medycyny wewnetrznej. 1998;99(6):452–61.
15. S. Alagesan, Arumuga P. Mohan. A study on peripheral nerve dysfunction in chronic kidney disease. IOSR journal of dental and medical sciences 2016; 15(5): 22-26.
16. Sultan LI. Evaluation of the clinical and neurophysiologic parameters of peripheral nerve functions in uremic Egyptian patients. Egypt J Neurol Psychiatr Neurosurg. 2007;44:473–87.
17. Babu MM, Kiran MR, Ravindra K, Srinivas V, Kandregula P, Vardhan RV, et al. Clinical manifestation and prevalence of peripheral neuropathy and nerve dysfunction in patients with chronic kidney disease. Int J Res Med Sci. 2015;3(2):451–5.
18. Jasti DB, Mallipeddi S, Apparao A, Vengamma B, Sivakumar V, Kolli S. A Clinical and Electrophysiological Study of Peripheral Neuropathies in Predialysis Chronic Kidney Disease Patients and Relation of Severity of Peripheral Neuropathy with Degree of Renal Failure. J Neurosci Rural Pract. 2017;8(4):516–24.
19. Tilki HE, Akpolat T, Coşkun M, Stålberg E. Clinical and electrophysiologic findings in dialysis patients. Journal of Electromyography and Kinesiology. 2009;19(3):500–8.
20. Jurčić D, Bilić A, Schwarz D, Oršanić D, Gabrić M, Špoljarić L, et al. Clinical course of uremic neuropathy in long-term hemodialysis. Collegium antropologicum. 2008;32(3):771–5.
21. Laaksonen S, Metsärinne K, Voipio-Pulkki LM, Falck B. Neurophysiologic parameters and symptoms in chronic renal failure. Muscle & nerve. 2002;25(6):884–90.