Incidence of Polyneuropathy among Uremic Patients Undergoing Hemodialysis: Cross-Sectional Study among Iraqis

Thaier Kareem Abdul- Aa'ama[1*], Fouad Shareef Dleikh[2], Riyadh Muhi Abbood Al-Saegh[3], Basim A. Abd Al-Ka'abi[4]

Abstract

Background: Peripheral neuropathy (PNP) is among the commonest neurological disorders. NP is a disorder of sensory or motor neurons. Peripheral NP impacts around 60-100% of cases admitted for dialysis units due to chronic kidney disease (CKD). In dialysis-dependent patients, a progressive uremic sensorimotor axonal NP is a well-known complication. Nevertheless, the precise polyneuropathy (PNP) among CKD patients has to be further investigated especially in our country.
Objectives: This cross-sectional study aimed to evaluate the incidence of polyneuropathy among Iraqi uremic patients undergoing hemodialysis.
Materials and Methods: This cross-sectional study was performed on patients 215 patients (99 women and 116 men). All participants were suffering from ESRD were assessed by expert specialists, aging 17-80 years, attending hemodialysis unit, receiving standardized maintenance hemodialysis. All patients had completed neurophysiological assessment in the same hospital, for sensory and motor nerves including median, ulnar, tibial, peroneal, and sural nerves, regardless of whether they had clinical findings of NP or not. SPSS (V-25) software was used for statistical analysis. A confidence level of 95% had considered significant.
Results: Mean age and weight of patients was (48.16 ±13.4 years and 66.9 ± 12.9 kg), respectively, and the mean duration of dialysis was 4.7 ± 1.4 years. The majority of patients (85.1%) had a frequency of dialysis three times/week. The prevalence of UNP was 63.7% among the studied candidates. More than half of patients (51.8%) presented with moderate UPN, (29.2%) with mild UPN, and (19. 0%) with severe UPN ($P<0.05$). There were significant differences between means of age and frequency of dialysis with the incidence of UPN.
Conclusion: Polyneuropathy is a very common complication in patients with uremia undergoing dialysis. Polyneuropathy is not associated with the frequency of dialysis, but with a duration of uremia.

Key Words: Uremia, Polyneuropathy, CKD, Chronic Kidney Diseases, Dialysis, Frequency, Hemodialysis, ESRD.
DOI Number: 10.14704/nq.2022.20.3.NQ22045 **NeuroQuantology 2022; 20(3):81-86**

Introduction

Neuropathy (NP) is a disorder of sensory or motor neurons, which might involve the soma, axon, or myelin sheath and hence categorized as, neural, axonal, or demyelinating neuropathology, respectively. NP could be acquired or hereditary; sensory, motor, or autonomic (Marchettini et al., 2006).

Corresponding author: Thaier Kareem Abdul- Aa'ama
Address: [1*]Medical Physiology, Al-Husseiny Teaching Hospital, Karbala, Iraq; [2]Department of Physiology, College of Medicine, University of Kufa, Iraq; [3]Department of Medicine, College of Medicine, University of Karbala, Holey Karbala, Iraq; [4]Department of Medical Physiology, College of Medicine, University of Babylon, Iraq.
E-mail: [1*]thaerkaromy970@gmail.com; [3]riadhmohiabud@yahoo.com; [4]basim6mol@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 30 December 2021 **Accepted:** 02 February 2022

The etiology of NP is a wide spectrum including dietary deficiencies, toxins, inflammatory, hereditary, metabolic, uremic, and others (Lehmann et al., 2020). Peripheral NP is among the commonest neurological disorders with a rate of 77/100,000/year and a prevalence of 2.4%, though this percentage number rises greatly in specific age groups since traumatic etiologies are not incorporated in this number (Misra et al., 2008, Lehmann et al., 2020).

Peripheral NP impacts around 60-100% of cases admitted for dialysis units due to chronic kidney disease (CKD). Uremic neuropathy (UNP) arises when kidney dysfunction prejudices glomerular filtration, causing the buildup of organic wastes. These patients will develop decreased glomerular filtration rate (GFR) typically with subsequent "end-stage renal disease (ESRD)" (Cooper et al., 1978). Generally, UNP distresses lower extremities in a distal symmetric fashion (Ghazan-Shahi et al., 2015, Sinha and Agarwal, 2013), and is owing to "length-dependent axonal degradation" and secondary local myelin injuries of (Ghazan-Shahi et al., 2015). In ESRD and dialysis-dependent patients, a progressive uremic sensorimotor axonal NP is a well-known complication (Tracy and Dyck, 2008). Nevertheless, the precise polyneuropathy (PNP) among CKD patients has to be further investigated especially in our country.

This cross-sectional study aimed to evaluate the incidence of polyneuropathy among Iraqi uremic patients undergoing hemodialysis.

Materials and Methods

This cross-sectional study was performed on patients 215 patients (99 women and 116 men) recruited from the nephrology unit in Al-Husseiny Teaching Hospital at Karbala Governorate, during November 2020 and extended over a year. All participants were suffering from ESRD were assessed by expert specialists, aging 17-80 years, attending hemodialysis unit, receiving a standardized maintenance hemodialysis regimen consisting of twice to thrice-weekly sessions, for 3-4 hours per session for a total average of 12 hours a week for more than 3 months. All participants were subjected to thorough medical history, general physical examination, and neurological examination before dialysis. Informed consent from each applicant was taken before being involved in the work. The entire work was authorized and approved by the health institute of Karbala.

All patients had completed neurophysiological assessment in the same hospital, for sensory and motor nerves including median, ulnar, tibial, peroneal, and sural nerves, regardless of whether they had clinical findings of NP or not.

Patients with preexisting NP before the diagnosis of CKD were excluded. As well, patients with NP disorders like inherited or autoimmune, collagen vascular disorders, amyloidosis, any primary neurologic disorder, and those on immunosuppressants and steroids, all were excluded from the study. The presence and severity of NP were assessed using "Baba's classification" (Baba et al., 2018).

Continuous variables were reported as means ± SD, while the categorical variables were addressed as numbers and percentages. The independent-samples t-test was applied for the continuous variables and the chi-square test for the categorical ones. In addition to that, correlation analyses were done between all the continuous variables to report the strength of the relationship between them. SPSS (V-25) software was used for statistical analysis. A confidence level of 95% had considered significant.

Results

Table-1 shows the distribution of patients according to study variables including (age, weight, and gender). The mean age of patients was (48.2 ± 13.4) years, the minimum age was 18 years and the maximum age was 80 years. The mean weight of patients was (66.9 ± 12.9) kg, minimum weight was 32 kg and maximum weight was 102 kg.

Table 1. The Distribution of patients according to study variables (N=215)

Age/years		Mean (SD) 48.2 ± (13.4)	Min – max (18.0 - 80.0)
Weight/kg		Mean (SD) 66.9 ± (12.9)	Min – max (32.0 - 102.0)
Duration/years		Mean (SD) 4.7 ± (1.4)	Min – max (1.0 – 6.5)
Gender	Male	116	54.0%
	Female	99	46.0%
Total		215	100.0%

Figure-1 shows the distribution of patients according to the duration of hemodialysis including

(< 1 year, 1-3 years, 3-5 years, and > 5 years). About one-third of patients (N=76, 35.3%) presented with a duration of hemodialysis (1-3 years), (N=59, 27.5%) of patients presented with a duration of hemodialysis (3-5 years), (N=44, 20.5%) of patients presented with a duration of hemodialysis (> 5 years) and only (N=36, 16.7%) of patients presented with a duration of hemodialysis (< 1 year).

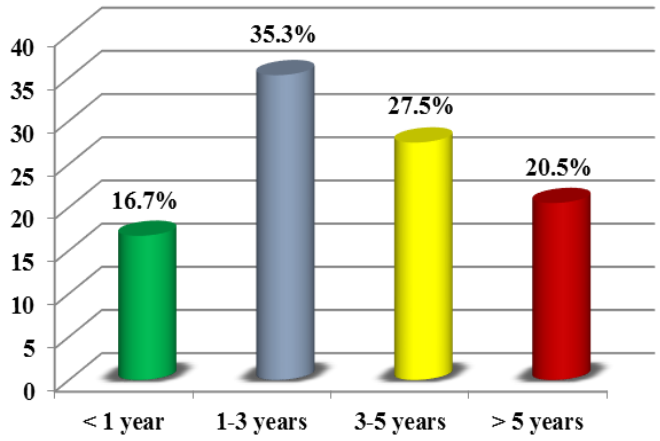

Figure 1. Distribution of patients according to the duration of hemodialysis (N=215)

Figure-2 shows the distribution of patients according to the frequency of hemodialysis including (twice per week, three times per week, and four times per week). Majority of patients (N=183, 85.1%) presented with the frequency of hemodialysis (three times per week), (N=27, 12.6%) of patients presented with the frequency of hemodialysis (twice per week) and only (N=5, 2.3%) of patients presented with the frequency of hemodialysis (four times per week).

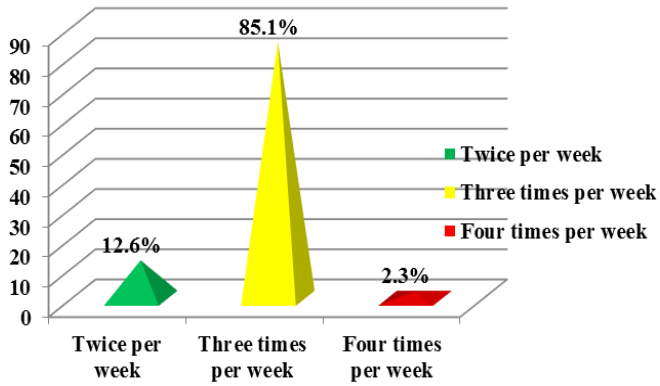

Figure 2. Distribution of patients according to the frequency of hemodialysis (N=215)

Figure-4 shows the distribution of patients according to uremic polyneuropathy. Uremic polyneuropathy presented in (N=137, 63.7%) of patients.

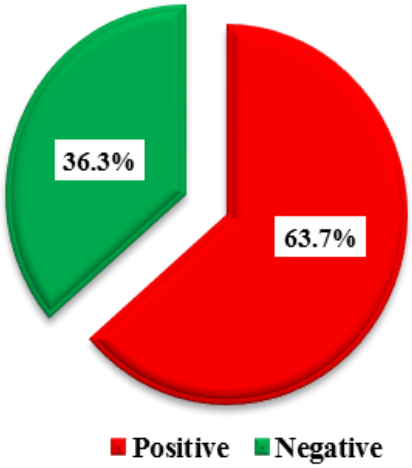

Figure 4. Distribution of patients according to uremic polyneuropathy (N=215)

Figure-5 shows the distribution of patients with uremic polyneuropathy according to severity including (mild polyneuropathy, moderate polyneuropathy, and severe polyneuropathy). More than half of patients (N=71, 51.8%) presented with moderate uremic polyneuropathy, (N=40, 29.2%) of patients presented with mild uremic polyneuropathy, and (N=26, 19. 0%) of patients presented with severe uremic polyneuropathy (P<0.05).

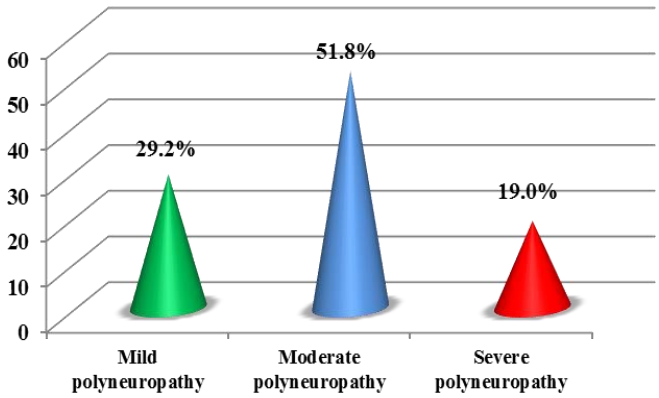

Figure 5. Distribution of patients with uremic polyneuropathy according to severity (N=137)

Table 3. There were significant differences between means of age and frequency of dialysis with the incidence of UPN. There was a nonsignificant association of weight, gender, and frequency of hemodialysis with uremic polyneuropathy

Study variables	Uremic polyneuropathy		Total	P-value
	Positive (N=137)	Negative (N=78)		
Age (years)	52.8 (12.4)	40.00 (11.1)	215	0.001
Weight (kg)	67.60 (12.27)	65.88 (13.88)	215	0.3
Gender				
Male	80 (58.4)	36 (46.2)	116 (54.0)	0.08
Female	57 (41.6)	42 (53.8)	99 (46.0)	
Frequency of hemodialysis				
Twice / week	17 (12.4)	10 (12.8)	27 (12.6)	1.0
Three times/week	117 (85.4)	66 (84.6)	183 (85.1)	
Four times/week	3 (2.2)	2 (2.6)	5 (2.3)	
Duration of hemodialysis				
< 1 year	17 (12.4)	19 (24.4)	36 (16.7)	
1-3 years	48 (35.1)	28 (35.9)	76 (35.3)	0.05
3-5 years	38 (27.7)	21 (26.9)	59 (27.5)	
>5 years	34 (24.8)	10 (12.8)	44 (20.5)	

Discussion

This cross-sectional study was prearranged to evaluate the incidence of polyneuropathy among Iraqi uremic patients undergoing hemodialysis. Uremic polyneuropathy was very common, presented in around 2/3rd of the involved patients (63.7%, N=137). More than half of patients (N=71, 51.8%) presented with moderate polyneuropathy, and less than 1/5th (N=26, 19. 0%) of patients presented with severe uremic polyneuropathy (P<0.05). A similar finding was reported by a retrospective Turkish study involving 36 patients on peritoneal dialysis (Taner Basturk, 2017). Another recent Egyptian study based on 30 children with uremia, revealed comparable findings (Mohammed Fathy Hassan Mohammed, 2021). In the meantime, another Egyptian study involved 60 uremic adults on regular dialysis, exhibited lower incidence rates of polyneuropathy. The clinical neuropathy was reported in 33 patients (55%), while electrophysiological study manifested by all of the clinically apparent set compared to 92.5% of the clinically in-apparent set (Nillie Ezzeldin, 2018). Moreover, a larger cohort from the USA included 1121 elders with ESRD showed that (15.6%) of the total applicants had a higher chance (2.37 times) to get new motor neuropathic findings. As well, ESRD had a higher chance (2.02 times) of worsening of - but not - with the progress of new monofilament insensitivity (Simit Doshi, 2020). On the same line, other recent Indian research, included 200 adults with ESRD on dialysis, exposed that incidence and severity of PN rise as renal impairment deteriorate (Jasti DB, 2019).

The pathogenesis of neuronal injury uremia is expected to be multifactorial. Nevertheless, the predicted mechanisms may be divided into two evolving premises, specifically neurodegenerative and vascular postulates (Arnold et al., 2016).

Many uremic toxins have been inspected for a possible deleterious neuronal in the milieu of ESRD. Neurovascular interrelations have been proposed for numerous compounds such as uric acid (Amir Al-Mumin, 2020, Arnold et al., 2016), indoxyl sulfate, p-cresyl sulfate (Watanabe et al., 2014). IL-1β and tumor necrosis factor-α are important multipurpose cytokines generally involved in systemic inflammatory responses (Al-Hindy et al., 2021, Amjed H. Abbas, 2021, Hayder Abdul-Amir Alhindy and Mazin J. Mousa Enas K. Alkhazraji, 2021) and both interacted in numerous pathologies including uremia (Arnold et al., 2016). Cystatin-C is a new marker of renal function (Abed, 2020, Asseel K. Shaker, 2020), the researchers recently have verified that high concentrations of cystatin-C are associated with lower cognitive scores and neurodegeneration via amyloid plaque synthesis though further studies are requisite (Yaffe et al., 2014).

On the other hand, vascular postulate based on the fact that the uremic cases may present with a high prevalence of non-classical cardiovascular risk factors like metabolic derangements, mostly related to phosphate and calcium, hypercoagulability, and oxidative stress (Simões E Silva et al., 2019), and urate levels that believed to aggravate endothelial dysfunction and worsen atherosclerosis (Hayder

Abdul-Amir Maki Al-Hindi, 2019, Hajir Karim Abdul-Husseein, 2020, Vanholder et al., 2018).

In this study, the age increment of the candidates had a significant impact on the incidence of UNP (P-0.001), a finding that was supported by several other scholars (Simit Doshi, 2020). Several preceding investigations have revealed a higher prevalence of vasculopathy (SV., 2010), neuropathy, and nephropathy with increasing ages (Le Floch et al., 2014). Meanwhile, other studies fail to show such association (Satu Laaksonen, 2002).

There was no sex preponderance among the studied cases similar to other studies (Basturk et al., 2017, Simit Doshi, 2020). The majority of the candidates were on dialysis for more than 1 year (83.7%) and had hemodialysis three sessions per week (85.3%). However, the duration of the dialysis for the study participants generally was shorter than the durations reported in international reports. This might be due to poor compliance or lost patients. There was a significantly higher incidence of UNP with increased duration of renal impairment, but no observed differences in the incidence of UNP according to the frequency of hemodialysis per week. UNP was a common presentation and its occurrence rises with the increase in dialysis duration among Egyptian adults (Nillie Ezzeldin, 2018). Contrarily, dialysis duration and effectiveness were not linked with the incidence of UNP in a prior revision (Satu Laaksonen, 2002).

Thus, early identification and management of neuropathy in mild ESRD is plausible and may signify a window of a prospect to moderate its impact in advanced stages. Future works should approve this relation and define if early recognition of neural impairments may initiate preventive measures to improve quality of life in uremic patients.

Conclusion

Polyneuropathy is a very common complication in patients with uremia undergoing dialysis. Polyneuropathy is not associated with the frequency of dialysis, but with the duration of uremia.

Funding: Self-funding.

Declaration of interest: The authors did not report any conflicts of interest, and they are alone responsible for its content and writing.

References

Abed DA, Jasim R, Al-Hindy HAA, Obaid AW. Cystatin-C in patients with acute coronary syndrome: Correlation with ventricular dysfunction, and affected coronary vessels. *Journal of Contemporary Medical Sciences* 2020; 6(1): 26-31.

Al-Hindy HA, Al-Athari AJ, Mousa MJ, Hameed SJ, Obeed SH. The utility of serum IL-1β and CRP together with fractional exhaled Nitric Oxide in the diagnosis of asthma in adults. *NeuroQuantology* 2021; 19(8): 119-124.

Al-Mmumin A, Al-Hindy HAAM. Hyperuricemia Has a Deleterious Role in Patients with Acute Coronary Syndrome Presented with Poor Oral Hygiene. *International Journal of Pharmaceutical Research* 2020; (Supplementary Issue 1): 1196-1202.

Abbas AH, Rasheed MA, Al-Hindy HAA, Mousa MJ, Al-Shalah HAA. The role of serum IL-1β in combination with fractional exhaled nitric oxide in the diagnosis of adult bronchial asthma. *NeuroQuantology* 2021; 19(8): 13-19.

Arnold R, Issar T, Krishnan AV, Pussell BA. Neurological complications in chronic kidney disease. *Journal of the Royal Society of Medicine Cardiovascular Disease* 2016; 5: 1-13.

Shaker AK, Al-Saad R, Jasim R, Al-Hindy HAA M. Biochemical significance of cystatin-C and high-sensitive CRP in patients with acute coronary syndrome; any clinical correlation with diagnosis and ejection fraction. *Systematic Reviews in Pharmacy* 2020; 11(3): 301-308.

Baba T, Kaneko K, Homma Y, Ochi H, Ozaki Y, Watari T, Matsumoto M. The Baba classification focused on implant designs is useful in setting the therapeutic strategy for interprosthetic femoral fracture. *European Journal of Orthopaedic Surgery & Traumatology* 2018; 28(2): 247-254.

Basturk T, Koc Y, Kayalar AO, Yilmaz F, Hasbal NB, Sakaci T, Unsal A. Frequency of polyneuropathy in patients on long term peritoneal dialysis treatment. *Journal of Clinical and Diagnostic Research: JCDR* 2017; 11(6): OC37- OC40.

Cooper JD, Lazarowitz VC, Arieff AI. Neurodiagnostic abnormalities in patients with acute renal failure: Evidence for neurotoxicity of parathyroid hormone. *The Journal of Clinical Investigation* 1978; 61(6): 1448-1455.

Ghazan-Shahi S, Koh TJK, Chan CT. Impact of nocturnal hemodialysis on peripheral uremic neuropathy. *BMC nephrology* 2015; 16(1): 1-4.

Abdul_Husseein HK, Dleikh FS, Al-Aaraji AJ, Al-Hindy HAAM, Mousa MJ. Biochemical causal-effect of circulatory uric acid, and HSCRP and their diagnostic correlation in admitted patients with ischemic heart diseases. *Journal of Cardiovascular Disease Research* 2020; 11(2): 25-31.

Alkhazraji EK, Alkhafaji AA, Alzughaibi MA, Alhindy HAA, Mousa MJ. Positive Correlation of Circulating Tumor Necrosis factor-alpha (TNFa) with Spirometric Pulmonary Tests in Adult Asthmatic Patients. *Biochemical and Cellular Archives* 2021; 21(Supplement 1): 2605-2610.

Al-Hindi HAAM, Sudan A, Abdul-Razzaq SA. Correlation of on Admission Levels of Serum Uric Acid with Acute Myocardial Infarction: Case: Control Study. *Journal of Global Pharma Technology* 2019; 11(7): 289-294.

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

*e*ISSN 1303-5150

neuropathy with degree of renal failure. *Journal of neurosciences in rural practice* 2017; 8(04): 516-524.

Le Floch JP, Doucet J, Bauduceau B, Verny C. Retinopathy, nephropathy, peripheral neuropathy and geriatric scale scores in elderly people with Type 2 diabetes. *Diabetic medicine* 2014; 31(1): 107-111.

Lehmann HC, Wunderlich G, Fink GR, Sommer C. Diagnosis of peripheral neuropathy. *Neurological research and practice* 2020; 2(1): 1-7.

Marchettini P, Lacerenza M, Mauri E, Marangoni C. Painful peripheral neuropathies. *Current neuropharmacology* 2006; 4(3): 175-181.

Misra UK, Kalita J, Nair PP. Diagnostic approach to peripheral neuropathy. *Annals of Indian Academy of Neurology* 2008; 11(2): 89-97.

Rabeea MM, Hassan HA, Elzamarany EHM. Neurophysiologic Study in Children with End Stage Renal Disease on Regular Hemodialysis. *Al-Azhar International Medical Journal* 2021; 2(12): 28-34.

Ezzeldin N, Abdel Galil SM, Said D, Kamal NM, Amer M. Polyneuropathy associated with chronic hemodialysis: Clinical and electrophysiological study. *International Journal of Rheumatic Diseases* 2019; 22(5): 826-833.

Laaksonen S, Metsärinne K, Voipio-Pulkki LM, Falck B. Neurophysiologic parameters and symptoms in chronic renal failure. *Muscle & nerve* 2002; 25(6): 884-890.

Doshi S, Moorthi RN, Fried LF, Sarnak MJ, Satterfield S, Shlipak M, Strotmeyer ES. Chronic kidney disease as a risk factor for peripheral nerve impairment in older adults: A longitudinal analysis of Health, Aging and Body Composition (Health ABC) study. *PloS one* 2020: 15(12).

Simoes e Silva AC, Miranda AS, Rocha NP, Teixeira AL. Neuropsychiatric disorders in chronic kidney disease. *Frontiers in pharmacology* 2019.

Sinha AD, Agarwal R. Chronic renal disease progression: treatment strategies and potassium intake. *In Seminars in nephrology* 2013; 33(3): 290-299.

McQuillan R, Jassal SV. Neuropsychiatric complications of chronic kidney disease. *Nature Reviews Nephrology* 2010; 6(8): 471-479.

Basturk T, Koc Y, Kayalar AO, Yilmaz F, Hasbal NB, Sakaci T, Unsal A. Frequency of polyneuropathy in patients on long term peritoneal dialysis treatment. *Journal of Clinical and Diagnostic Research: JCDR* 2017; 11(6): OC37- OC40.

Tracy JA, Dyck PJB. The spectrum of diabetic neuropathies. *Physical medicine and rehabilitation clinics of North America* 2008; 19(1): 1-26.

Vanholder R, Pletinck A, Schepers E, Glorieux G. Biochemical and clinical impact of organic uremic retention solutes: a comprehensive update. *Toxins* 2018: 10(1).

Watanabe K, Watanabe T, Nakayama M. Cerebro-renal interactions: impact of uremic toxins on cognitive function. *Neurotoxicology* 2014; 44: 184-193.

Yaffe K, Kurella-Tamura M, Ackerson L, Hoang TD, Anderson AH, Duckworth M, Go AS, Krousel-Wood M, Kusek JW, Lash JP, Ojo A, Robinson N, Sehgal AR, Sondheimer JH, Steigerwalt S, Townsend RR. Higher levels of cystatin C are associated with worse cognitive function in older adults with chronic kidney disease: the chronic renal insufficiency cohort cognitive study. *Journal of the American Geriatrics Society* 2014; 62(9): 1623-1629.

Hasan KH, Mhawes AJ. Use diode laser to estimate foot diabetes disease. *NeuroQuantology* 2020; 18(4): 27-30.