DOI: 10.7860/JCDR/2017/24572.10101

Original Article

Internal Medicine Section

Frequency of Polyneuropathy in Patients on Long Term Peritoneal Dialysis Treatment

TANER BASTURK[1], YENER KOC[2], ARZU OZDEMIR KAYALAR[3], FIGEN YILMAZ[4], NURI BARIS HASBAL[5], TAMER SAKACI[6], ELBIS AHBAP[7], ABDULKADIR UNSAL[8]

ABSTRACT

Introduction: Uremic polyneuropathy is very common among patients with Chronic Kidney Disease (CKD). The patients have electrophysiologic signs of impaired nerve function, although a lower percentage of patients are symptomatic. Electrophysiological parameters are quantitative indices of Polyneuropathy (PNP) severity.

Aim: To assess the frequency of PNP in patients on long term Peritoneal Dialysis (PD) treatment.

Materials and Methods: Twenty three PD patients were analysed, who were receiving dialysis for at least five years and the study population divided into two groups according to duration of PD treatment. Group 1 consisted of the patients who were dialysed for at least 10 years and Group 2 consisted of patients who were dialysed for five to nine years. Patients who switched from Haemodialysis (HD) to PD and patients with coexisting diseases that could lead to disturbances in nerve conduction were excluded from the study. PNP was diagnosed when slowing of Nerve Conduction Velocity (NCV) and/or lengthening of distal latencies and/or decrease in amplitude of muscle action potential were present in two or more nerves and longer F wave response was present in one or two nerves. Carpal Tunnel Syndrome (CTS) was diagnosed if slowing of NCV and/or decrease in amplitude of muscle action potential and/or lengthening of distal latency of either sensory or motor median nerve present.

Results: PNP was observed in 17 of the patients {73.9%; Group 1 (n=10) and Group 2 (n=7)}. Mixed type sensory motor neuropathy was diagnosed in nine patients from Group 1 and five patients from Group 2; one patient from Group 1 had demyelinating PNP affecting motor and sensory nerves; one patient from Group 2 had axonal PNP affecting motor and sensory nerves. From Group 1, two patients had CTS related to PNP and one patient had CTS without PNP. The results of motor conductivity testing showed lower conduction velocity for left popliteal nerve in Group 1 and Group 2 patients (13.85±2.17 ms, 4.80±1.11 ms, p=0.01). In both groups, mean motor and sensory latency, amplitude and velocity of other nerves were not found to be significantly different (p>0.05).

Conclusion: PNP is a common complication in long term PD patients. Over five years of treatment, frequency of PNP and CTS do not increase with duration of dialysis.

Keywords: End-stage renal disease, Electrophysiological parameters, Renal replacement therapy

INTRODUCTION

PD and HD are done for patients with End Stage Renal Disease (ESRD). Their life time gets extended but these procedures are not devoid of complications [1]. The most frequent long term dialysis complications are cardiovascular disease, peripheral neuropathy, parathyroid adenoma and acquired cystic disease of the kidney [1,2]. Uremic polyneuropathy is common among patients with CKD. Electrophysiologic signs of impaired nerve functions are seen in 60-100% of dialysis patients, though lesser of these patients show symptoms [3-5]. Electrophysiological parameters are quantitative indices of PNP severity. Typically presenting with a distal symmetric pattern with greater involvement of the lower extremities compared to the upper extremities [6]. A correlation has been found between electrophysiologic changes of PNP or CTS and duration of ESRD and dialysis [5]. The aim of our study was to assess frequency of PNP in patients on long term PD treatment.

MATERIALS AND METHODS

In this retrospective observational study, we evaluate the records of 388 patients with ESRD for whom PD therapy was started in PD unit of Sisli Hamidiye Etfal Training and Research Hospital between January 2001 and March 2015 to find out the patients who has received PD therapy longer than five years. Total 23 patients were enrolled in the study and divided into two groups according to the duration of PD treatment. Group 1 consisted of the patients who were dialysed for 10 and more years and Group 2 consisted of patient who were dialysed for five to nine years. Electrophysiological studies were conducted on these 23 patients.

Patients who have been switched from HD to PD or vice versa, followed up in different centers and died after five years of commencement of dialysis, and with history of coexisting diseases such as diabetes mellitus, systemic lupus erythematosus, systemic vasculitides, multiple myeloma, amyloidosis, peripheral vascular disease, deficiency of vitamin B12 and B6 were excluded from the study. Detailed history was elicited pertaining patients' neurological symptoms such as tingling and prickling sensation in the legs, paresthesia, hyperalgesia, weakness, numbness of lateral four fingers for compressive neuropathies, pain and stiffness of the hands. No patients took medications such as NSAIDs or specific nerve pain medications for pain.

We retrieved demographic (age, gender) and biochemical data {including serum creatinine, calcium, phosphorus, potassium, albumin, intact parathyroid hormone (iPTH)} of all patients were recorded. The dialysis data included dialysis mode Automated Peritoneal Dialysis (APD) (10 L-15 L exchanges per day) and Continuous Ambulatory Peritoneal Dialysis (CAPD) (4-5 x 2-2.5L exchanges per day). Blood samples were drawn from the subjects after overnight fasting. The biochemical parameters serum glucose, urea, and creatinine were determined using standard biochemical methods. Adequacy of dialysis was calculated from 24-hour

dialysate and urine collections for urea and creatinine. Peritoneal creatinine clearance (pCcr) was corrected to a body surface area of 1.73 m^2 and urea clearance was expressed as dialysis dose (Kt/V, where K is solute clearance, t is duration of the exchange, and V is the volume of dialysate drained at the end of the exchange) using the Watson formula for body water. Renal creatinine clearance (rCcr) was calculated from the mean of creatinine and urea clearances corrected to a body surface area of 1.73 m^2, while total Ccr was calculated as the sum of pCcr and rCcr. Total weekly Ccr and weekly pCcr were expressed in liters per 1.73 m^2. Residual Ccr of 1 ml/minute is equivalent to a weekly clearance of 10 l/1.73 m^2 [7].

Nerve conduction studies were performed using Nihon Kohden equipment at room temperature. Using standard conduction techniques bilateral median, ulnar, peroneal and tibial motor nerves and median, ulnar, superficial peroneal, sural sensory nerves were evaluated. Signs and symptoms related to uremic PNP were assessed and electrophysiological studies for diagnosis of PNP and CTS had been performed by the same physician and the same device. Distal latency, amplitude and NCV of motor and sensory nerves and F waves minimal latency of all motor nerves were measured. PNP was diagnosed when slowing of nerve conduction velocity and/or decrease in amplitude of muscle action potential and/or lengthening of distal latencies were present in two or more nerves and longer F wave response was present in one or more nerves. CTS were diagnosed if slowing of NCV and/or decrease in amplitude of muscle action potential and/or lengthening of distal latency of either sensory or motor median nerve was present.

STATISTICAL ANALYSIS

Statistical analysis was done by Scientific Package for Social Science (version 17.0; SPSS Inc., Chicago, IL, USA). All continuous data were expressed as mean±SD and were analysed by unpaired t-test. Categorical data were expressed as number (percentage) and were analysed by X^2 test. Correlation analysis were tested by Pearson's correlation statistics for analysing parametric values and Spearman's rho test was used for analysing non parametric values. Differences were considered statistically significant if p-value was less than 0.05.

RESULTS

A total of 23 patients were included into the study. Participants predominantly were female (73.9%) with a mean age of 40.6±11.6 years and mean follow up of 9.3±3.48 years. Hypertension (31.8%), glomerulonephritis (18.18%), tubulointerstitial nephritis (18.18%), polycystic kidney diseases (9.09%) and unknown aetiology (22.72%) were the leading causes of ESRD. Seven PD patients (30.4%) were treated with CAPD, 16 (69.6%) of them were treated with APD.

In Group 1; 8 of 12 patients were female, mean age of PD was 39.5±10.2 years and mean duration of PD was 11.5±3.3 years. In Group 2; 9 of 11 patients were female, mean age of PD was 41.8±15.3 years and mean duration of PD was 6.82±1.07 years. There was no statisically difference between the two groups regarding demographic, clinical and laboratory parameters, and in Group 1 patients had longer duration of dialysis than Group 2 patients (p<0.001) [Table/Fig-1].

Five patients (three in Group 1 and two in Group 2) had complained of weakness and tingling and prickling sensation in the legs. None of them had loss of deep tendon reflexes, abnormal or absent reflexes and impaired sensation on physical examination.

PNP diagnosed based on the above described criteria, was found in 17 PD patients (73.9%; 10 in Group 1 and seven in Group 2). Fifteen patients (nine patients in Group 1 and six patients in Group 2) had mixed type sensory motor neuropathy, one patient in Group 1 had demyelinating PNP effecting motor and sensory nerves, one patient in Group 2 had axonal PNP effecting motor an sensory nerves. Two patients in Group 1 had CTS related to PNP and one patient from Groups 1 had CTS without PNP. Only one patient in Group 1 had numbness of lateral four fingers, pain and stiffness of the hands and thenar atrophy.

Parameters	All patients (n:23) Mean±SD	Group 1 (n:12) Mean±SD	Group 2 (n:11) Mean±SD	p-value
Mean age (years)	40.6±12.6	39.5±10.2	41.8±15.3	0.68
Gender (female/male)	18/5	8/4	9/2	0.69
Mean follow up time (years)	9.3±3.4	11.58±3.37	6.82±1.07	<0.001
Kt/V_{Urea}	2.66±1.32	3.16±1.15	2.84±0.56	0.42
Body mass index (kg/m^2)	22.2±4.6	21.6±4.9	23.5±4.6	0.36
Urea level, (mg/dL)	94.0±36.4	120±27	117±28	0.20
Creatinine level, (mg/dL)	8.6±1.5	8.84±1.9	8.85±1.1	0.78
Potassium, (ng/ml)	4.64±0.45	4.5±0.7	4.8±0.6	0.39
Calcium level, (mg/dL)	8.9±1.1	8.66±1.52	9.0	0.86
Phosporus level, (mg/dL)	4.1±1.3	4.52±1.1	4.14±0.97	0.39
Parathyroid hormone level, (pg/dL)	564.0±530.6	641.1±656	508.8±341	0.54

[Table/Fig-1]: Demographic and clinical data of patients.

All of the patients had two or more abnormal electrophysiologic parameters. The results of motor conductivity testing showed lower latency for popliteal nerve in both Group 1 and Group 2 patients (13.85±2.17 ms, 4.80±1.11 ms, p < 0.001). In both groups mean motor and sensory latency, amplitude and velocity of other nerves were not found to be significant (p>0.05) [Table/Fig-2,3].

DISCUSSION

Neuropathy occurs in minimum 65% of patients who are about to begin dialysis for CKD and is perhaps the most common neurological consequence of chronic uremia [8]. However, patients already being adequately dialysed may also develop PNP, although the PNP is often subclinical and detectable only by electrophysiologic studies among these patient group [9,10].

PNP due to uremic toxins is a distal, motor and sensory PNP with segmental demyelination, axonal degeneration and segmental re-myelination [11]. PNP affected 30% more women than men, predominantly in those over 40 years, and mononeuropathy was predominant in 65.8% of cases [6]. Santos et al., investigated 27 patients on HD treatment for six to sixty months and observed PNP in 92.6% of patients [12]. The common type of peripheral neuropathy observed in this study was mixed type sensory motor neuropathy and prevalence of this type of sensory motor neuropathy was 69.5%.

The pathophysiologic basis of uremic neuropathy is postulated to be due to retention of neurotoxic molecules in the middle molecular range, chronic hyperkalemic depolarization of nerve fibers, and prolonged nerve conduction velocities induced by high PTH [13-15].

The patients treated with PD had lower rates of uremic neuropathy despite having higher blood urea and creatinine concentrations. The lower neuropathy rate in the PD patients was thought to indicate that the substance responsible for neuropathy was better dialysed by the peritoneum than by the membranes used in HD. The clearance of middle molecules (500 to 2000 daltons) is greater with PD due to the increased time of dialysis [15]. Thus, more efficient middle molecule clearance could explain the seemingly better outcome with PD. This hypothesis has been criticized, because of the failure to consider the contribution of residual renal function which tends to

Parameters	Group 1 (n=12)				Group 2 (n=11)				Group 1 vs Group 2 (p-values)			
	Latency (ms) Mean ± SD	Amplitude Mean ± SD	NCV (m/s) Mean ± SD	F-wave (ms) Mean ± SD	Latency (ms) Mean ± SD	Amplitude Mean ± SD	NCV (m/s) Mean ± SD	F-wave (ms) Mean ± SD	Latency (ms)	Amplitude	NCV (m/s)	F-wave (ms)
Median, Left	3.58±0.77	11.27±5.49	51.94±6.45	27.87±3.28	3.59±0.63	10.26±2.26	52.03±3.40	26.43±2.67	0.975	0.576	0.969	0.272
Median, Right	3.73±0.73	12.16±5.20	51.36±5.80	28.48±4.35	3.69±1.02	11.81±3.84	52.41±5.33	27.23±3.32	0.921	0.861	0.657	0.452
Ulnar, Left	2.63±0.40	13.98±3.71	52.32±8.73	27.92±3.82	2.47±0.27	13.78±3.33	53.34±9.51	26.20±3.06	0.279	0.894	0.797	0.258
Ulnar, Right	2.63±0.40	13±3.97	54.95±5.54	27.80±3.91	2.45±0.35	12.54±2.84	58.15±6.83	26.37±2.82	0.553	0.752	0.644	0.330
Tibial Left (Popliteal)	13.85±2.17	5.75±2.70	43.57±3.80	50.46±5.59	4.80±1.11	7.40±3.0	43.50±6.31	48.47±5.99	<0.001	0.189	0.977	0.477
Tibial Right (Popliteal)	14.04±1.67	5.75±2.70	40.73±5.23	50.82±6.52	13.67±3.50	6.86±4.35	41.26±7.58	45.58±17.24	0.760	0.174	0.851	0.359
Peroneal Left	4.05±1.20	3.58±1.93	43.40±7.17	44.17±12.56	4.43±1.98	4.92±1.76	43.14±6.95	47.45±5.53	0.594	0.114	0.932	0.504
Peroneal Right	3.83±0.59	4.09±2.07	40.96±4.79	44.21±15.64	4.43±1.98	5.02±1.75	43.30±6.56	47.73±7.27	0.713	0.282	0.360	0.618

[Table/Fig-2]: Motor nerve conduction values of all patients.

Parameters	Group 1 (n=12)			Group 2 (n=11)			Group 1 vs Group 2 p-values		
	Latency (ms)	Amplitude	NCV (m/s)	Latency (ms)	Amplitude	NCV (m/s)	Latency (ms)	Amplitude	NCV (m/s)
Median, Left	2.91±0.71	28.11±11.66	44.84±8.03	2.72±0.60	31.14±11.60	45.64±7.23	0.507	0.548	0.809
Median, Right	3.10±0.73	28.50±12.74	41.48±7.29	2.70±0.64	29.39±13.16	46.19±7.63	0.193	0.874	0.155
Ulnar, Left	2.44±0.39	27.69±7.26	46.56±6.57	2.19±0.20	26.37±9.27	47.17±3.91	0.088	0.714	0.795
Ulnar, Right	2.34±0.40	33.49±6.97	48.05±6.65	2.17±0.28	27.88±9.93	48.45±3.61	0.260	0.141	0.863
Sural Left	3.38±0.34	8.60±3.80	43.63±4.87	3.49±0.52	9.00±4.31	44.66±4.64	0.568	0.837	0.650
Sural Right	3.40±0.41	11.42±4.09	42.23±5.13	3.52±0.44	9.52±3.70	42.63±3.61	0.557	0.306	0.847
Peroneal Left	2.20±0.26	13.47±7.29	43.78±4.33	2.25±0.13	12.08±3.50	44.01±3.41	0.649	0.655	0.913
Peroneal Right	2.59±0.21	11.14±6.13	42.18±3.28	2.69±0.43	16.18±8.16	42.90±4.55	0.562	0.180	0.722

[Table/Fig-3]: Sensory nerve conduction values of all patients.

be better maintained in those on PD. Recent studies comparing HD and PD have noted a greater decline in motor nerve conduction and vibration sensation with PD. Thus, the pathogenetic importance of middle molecule retention remains unresolved [15,16].

The only middle molecule for which some evidence of neurotoxicity exists is PTH, with some studies suggesting a link between PTH and the neurological complications of ESRD. PTH has been shown to prolong motor nerve conduction velocities in animal studies although human studies of the effect of PTH on peripheral nerves have yielded conflicting results, with variable changes in motor nerve conduction velocity in patients with ESRD [17]. In our study, mean PTH level was 564±530 pg/dl and there was no significant correlation with PNP. Although, PTH levels were higher in Group 1 but there were no profound difference between Group 1 and Group 2 (p=0.54) [Table/Fig-1].

Prolonged exposure to hyperkalemia in dialysis patients may cause disruption of the normal ionic gradients and activate calcium-mediated damaging processes leading to axonal loss. Excitability studies also demonstrated that abnormalities of nerve function occurred at a level much lower than that required for cardiac toxicity, with patients manifesting axonal changes with serum K^+ concentrations in the high normal range (i.e., 4.9–5.0 mmol/l) [16]. Standard PD solutions contain no potassium and main driving force for the elimination of potassium is the diffusive gradient between blood and PD fluid. Peritoneal clearance for potassium averages about 17 ml/minute for APD, and approximately 7 ml/minute for CAPD [18]. Therefore, hyperkalemia is less common than hypokalemia in PD patients. In a local study by Szeto CC et al., the prevalence of hyperkalemia in a cohort of 266 patients was 3%, much lower than the prevalence of hypokalemia (20.3%). Mean potassium level was 4.64±0.45 mg/dL and there were no significant correlation between Group 1 and Group 2 [Table/Fig-1]. Hyperkalemia is not a widespread electrolyte disturbance in PD patients so that it may not have any contribution to pathophysiology of PNP in PD patients [19].

Nerves of uremic patients have shown to exist in a chronically depolarized state prior to dialysis with subsequent improvement and normalization of resting membrane potential after dialysis. Some studies have shown minor changes during follow up periods ranging from one month to three years. In contrast, the peripheral nerve function deteriorated in some other studies [20]. Rate of PNP in Group 2 was 63.6%, the rate increased to 83.3% in Groups 1, however no statistically significant difference was found between these two groups (p=0.28). After five years of PD, frequency of the peripheral neuropathy did not increase.

Reduction in peroneal nerve motor conduction velocity and prolongation of tibial F-wave minimum latencies have been established as sensitive indicators of neuropathy in ESRD patients [5]. CTS is the most common mononeuropathy in dialysis patients, with a reported prevalence of 6% to 31% [15]. CTS are the most common complication of Dialysis-Related Amyloidosis (DRA) and can occur due to accumulation of beta-2 microglobulin in carpal tunnel. Compression by calcium phosphate deposits (uremic tumoral calcinosis) may also contribute to CTS [21].

Kwon H-K et al., evaluated 120 patients with dialysis (64 HD and 48 PD) prospectively for CTS. In HD group, 18 patients were categorized as having clinical CTS and in PD group there were 11 patients with CTS. In PD group, 16 patients developed PN, four patients had CTS and eight patients had CTS and PN together [22]. In our study, prevalence of CTS was 18.7% and there was only one patient with sypmtoms related to CTS.

We did not have any electrophysiological studies in the first application so that we could not find out how many patients had CTS in the beginning of dialysis and the incidence rise with years of PD. Since, both PNP and CTS can cause pain and/or numbness of the hands, the differentiation of the two entities is important in the management of patients. We used separate electrodiagnostic criteria to diagnose the PN and CTS, where two patients of them had CTS related to PNP and one patient had CTS without PNP.

CONCLUSION

PNP is a common complication in long term PD patients. Over five years of treatment, frequency of PNP and CTS did not increase with duration of dialysis. The frequency of CTS did not increase as the severity of the peripheral neuropathy and the duration of ESRD and dialysis increased.

REFERENCES

[1] Tse KC, Lui SL, Lo WK. Comparison of long-term survival (beyond 12 years) in patients on peritoneal dialysis and on haemodialysis. Perit Dial Int. 2003;23(S2):S104–08.
[2] Kayalar AO, Basturk T, Koc Y, Yilmaz F, Caglayan FB, Sakaci T, et al. Comparison of long-term complications in patients on haemodialysis and peritoneal dialysis longer than 10 years. J Clin Diagn Res. 2016;10(2):OC05-8.
[3] Bolton CF, Young GB. Uremic neuropathy. In: Neurological Complications of Renal Disease, Butterworth (Ed), Boston 1990. pp.76.
[4] Baumgaertel MW, Kraemer M, Berlit P. Neurological complications of acute and chronic renal disease. Hanb Clin Neurol. 2014;119:383-93.
[5] Laaksonen S, Metsärinne K, Voipio-Pulkki LM, Falck B. Neurophysiologic parameters and symptoms in chronic renal failure. Muscle Nerve. 2002;25:884.
[6] Ramírez BV, Gómez PAB. Uremic neuropathy: A review. Int J Genet Mol Biol. 2012;3(11):155-60.
[7] Keshaviah P. Adequacy of peritoneal dialysis. In: Gokal R, Nolph KD, eds. The Textbook of Peritoneal Dialysis. Dordrecht, The Netherlands: Kluwer Academic; 1994:419–42.
[8] Babu MM, Kiran MR, Ravindra K, Sirinivas 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):451-55.
[9] Makkar RK, Kochar DK. Somatosensory Evoked Potentials (SSEPs), Sensory Nerve Conduction Velocity (SNCV) and Motor Nerve Conduction Velocity (MNCV) in chronic renal failure. Electromyogr Clin Neurophysiol. 1994;34:295–300.
[10] Bazzi C, Pagani C, Sorgato G, Albonico G, Fellin G, D'Amico G. Uremic polyneuropathy: a clinical and electrophysiological study in 135 short- and long-term hemodialysed patients. Clin Nephrol. 1991;35:176–81.
[11] Said G. Uremic neuropathy. Hanb Clin Neurol. 2013;115:607-12.
[12] Santos, Adriana Ondina Pestana. Peripheral neuropathy in patients in haemodialysis treatment. http://hdl.handle.net/10400.6/1104
[13] Toepfer M, Schiffl H, Fricke H, Lochmuller H, Held E, Pongratz D, et al. Inflammatory demyelinating neuropathy in patients with end-stage renal disease receiving continuous ambulatory peritoneal dialysis (CAPD). Perit Dial Int. 1998;18:172–76.
[14] Bansal VK, Bansal S. Nervous system disorders in dialysis patients. Handb Clin Neurol. 2014;119:395-404.
[15] Krishnan AV, Kiernan MC. Uremic neuropathy: Clinical features and new pathophysiological insights. Muscle Nerve. 2007;35(3):273-90.
[16] Krishnan AV, Pussel BA, Kiernan MC. Neuromuscolar disease in the dialysis patient: an update for the nephrologist? Seminars in Dialysis. 2009;22(3):267-78.
[17] Krishnan AV, Phoon RK, Pussell BA, Charlesworth JA, Bocstock H, Kiernan MC. Altered motor nerve excitability in end-stage kidney disease. Brain. 2005;128(Pt 9):2164-74.
[18] Krediet R. The physiology of peritoneal solute transport and ultrafiltration. In Gokal R, Khanna R, Krediet R, Nolph K. (Eds). Textbook of peritoneal dialysis. Dordrecht. Kluwer Academic Publishers. 2000:149-72.
[19] Szeto CC, Chow KM, Kwan BC, Leung CB, Chung KY, Law MC, et al. Hypokalemia in Chinese peritoneal dialysis patients: prevalence and prognostic implication. Am J Kidney Dis. 2005;46:128–35.
[20] Lindholm B, Tegner R. Deterioration of peripheral nerve function during continuous ambulatory peritoneal dialysis. Perit Dial Int. 1986;6-1:20-24.
[21] Cofan F, Garcia S, Combalia A, Segur JM, Oppenheimer F. Carpal tunnel syndrome secondary to uremic tumoral calcinosis. Rheumatology (Oxford). 2002;41:701-03.
[22] Kwon H-K, Pyun S-B, Cho WY, Boo CS. Carpal tunnel syndrome and peripheral polyneuropathy in patients with end stage kidney disease. J Korean Med Sci. 2011;26:1227-30.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.
2. Associate Professor, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.
3. Fellow, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.
4. Associate Professor, Department of Physical Treatment and Rehabilitation, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.
5. Fellow, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.
6. Specialist, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.
7. Associate Professor, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.
8. Professor, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Taner Basturk,
Associate Professor, Department of Nephrology, Sisli Hamidiye Etfal Training and Research Hospital Halaskargazi cad.,
Etfal sok., PK: 34371, Istanbuls, Turkey.
E-mail: tanerbast@yahoo.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Oct 03, 2016**
Date of Peer Review: **Nov 08, 2016**
Date of Acceptance: **Jan 13, 2017**
Date of Publishing: **Jun 01, 2017**