

## Research Article

# Clinical manifestation and prevalence of peripheral neuropathy and nerve dysfunction in patients with chronic kidney disease

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### ABSTRACT

**Background:** Chronic Kidney Disease (CKD) is recognized as a major health problem. Prevalence of CKD is rising continuously; mostly CKD is affecting the elderly aged population and/or patients with diabetes and hypertension. Present study was aimed to explore clinical manifestation and evaluate the prevalence of peripheral neuropathy and peripheral nerve dysfunction in CKD patients attending our hospital with reference to the severity and duration of the CKD.

**Methods:** The present cross sectional study was conducted in 74 patients affected with chronic kidney disease, of different age groups at the medical wards of King George Hospital, Visakhapatnam. The presence of peripheral nerve dysfunction was assessed by nerve dysfunction clinically (motor or sensory symptoms and signs) and electrophysiological nerve conduction studies.

**Results:** Out of 74 patients, 65% of study population was suffering from chronic kidney disease with peripheral nerve dysfunction. The peripheral nerves dysfunction was more prevalent in elder age (>65 years) subjects when compared to subjects with age <65 years. Moreover, the results shown that the rate of prevalence of peripheral nerves dysfunction was observed higher in subjects with longer duration of CKD. Male subjects were affected more when creatinine clearance is <15 ml/minute. Both sexes were affected equally when creatinine clearance is between 30-59 ml/minute.

**Conclusion:** This study enlightens the prevalence and clinical presentation of peripheral nerve dysfunction in patients with CKD. The CKD was found to cause peripheral neuropathy including overt and subclinical neuropathy, of which distal symmetrical sensory motor neuropathy was common in CKD. The prevalence of peripheral neuropathy was directly proportional to duration and severity of CKD.

**Keywords:** CKD, Creatinine, Neuropathy, Peripheral neuropathy

### INTRODUCTION

The Chronic Kidney Disease (CKD) is a worldwide public health problem and is a long term condition caused by kidney damage. The CKD leads to progressive and irreversible destruction of nephron mass, irrespective of cause. The eventual impact of severe reduction in nephron mass is an alteration in function of virtually

every organ system in the body.<sup>1</sup> CKD is a rapidly growing global health problem, with a prevalence of 15% in developed nations and peripheral neuropathy is most common complication with kidney disease.<sup>2</sup> The average prevalence has been reported around 11% in USA and Europe (excluding those on dialysis or with a functioning transplant).<sup>3</sup> CKD potentially affects all levels of the nervous system, from the CNS through to the Peripheral

Nervous System (PNS).<sup>4</sup> CKD is defined as the presence of kidney damage, manifested by abnormal albumin excretion or decreased kidney function, quantified by measured or estimated Glomerular Filtration Rate (GFR), that persists for more than 3 months.<sup>5,6</sup> There are different levels of chronic kidney disease which provides the basis of an international classification system (Table 1). Previous renal clinical guidelines have focused on patients with End-Stage Renal Disease (ESRD).<sup>7-9</sup> End-stage renal disease, also called established renal failure, is chronic kidney disease which has progressed so far that the patient's kidneys no longer function sufficiently and dialysis or transplantation become necessary to maintain life. In the US alone, more than 0.4 million individuals have end-stage kidney disease (stage 5 CKD) and the prevalence of advanced CKD requiring renal replacement therapy has been doubled in the last ten years.<sup>2</sup> The exact prevalence of CKD is remain unknown in India due to lack of renal registry but some community based studies have reported the prevalence of chronic kidney failure between 0.16-0.79%.<sup>3,10</sup>

The potential importance of peripheral nervous dysfunction in the CKD is highlighted by the worldwide mortality in End Stage Renal Disease (ESRD) patients as high as 20% per annum. Neuropathy occurs in minimum 65% of patients who are about to begin dialysis for chronic kidney disease and is perhaps the most common neurological consequence of chronic uremia.<sup>11,12</sup> From a neurological perspective, clinical features of CKD include weakness and length-dependent sensory impairment, which lead to functional disability, and, in patients with acute uremia, an altered mental state due to encephalopathy. Neuropathy may be manifested as encephalopathy, peripheral polyneuropathy, autonomic dysfunction, sleep disorders, and, less commonly peripheral mononeuropathy.<sup>12,13</sup> Certain causes of chronic kidney disease that also affect central and/or peripheral nervous system that amyloidosis, diabetes, systemic lupus erythematosus, polyarteritis nodosa, hepatic failure and peritoneal dialysis, hemodialysis and transplantation have revolutionized the prognosis of CKD in recent periods. Levels of urea, creatinine, parathyroid hormone (PTH), "middle molecules," and others have been correlated with reduction of Nerve Conduction Velocity (NCV) and peripheral manifestations of neuropathy. Symptoms of peripheral neuropathy generally do not present unless the GFR is under 12 to 20 mL/min, or unless the uremia has been present for at least six months. Encephalopathy may become evident with less prolonged impairment of kidney function and can be seen with acute decline in GFR, although the correlation of central nervous system manifestations with level of kidney function is poor. Autonomic neuropathy is present in 20-80% of patients with diabetic nephropathy, in 66% of patients with severely impaired kidney function (creatinine clearance <8 mL/min), and in 50% of patients on dialysis. Peripheral neuropathy as evaluated by NCV studies is present in 15-85% of individuals with decreased GFR. Sensory NCV is decreased in over 90% of patients,

whereas motor NCV is decreased in only 40%. Among patients on dialysis, objective evidence of neuropathy is present in 50-100% and the prevalence appears to increase with duration of dialysis.<sup>14</sup> Onset and severity of neuropathy is associated with the level of GFR; there is insufficient evidence to define a specific threshold level of GFR that is associated with an increased prevalence or severity of neuropathy.<sup>14</sup> Henceforth, the present study was aimed to evaluate prevalence and explore the clinical manifestation and severity of peripheral nerve dysfunction among patients with CKD.

## METHODS

### *Patients*

This descriptive cross sectional study was carried out at the medical wards of King George Hospital, Vishakhapatnam, during the period of March 2012 - October 2013. Total 74 patients of different age groups with proved clinical, bio-chemical parameters in favor of chronic kidney disease were included in study and the duration of renal failure varied from 3 months to 7 years. None of the patients included in this study were on dialysis.

### *Ethical clearance*

Ethics committee approval was obtained and study was conducted accordance with the guidelines of institutional ethics committee. Informed consent was obtained from each participant.

### *Inclusion & exclusion criteria*

Patients of different age groups with the chronic kidney disease having creatinine clearance <40 ml/minute, serum creatinine >2 mg% and ultrasound abdomen - kidney size < 9 cm were included in this study. Patients having diabetes mellitus, alcoholism, drug induced peripheral neuropathy, Hansen's disease were excluded from the study.

### *Methods*

The presence of peripheral nerve dysfunction was assessed by the nerve dysfunction clinically (Motor and sensory symptoms and signs) and electrophysiological studies - nerve conduction studies. Clinical features like peripheral sensory loss, pin & needle sensation, burning feet sensation, distal muscle weakness and distal reflex loss were taken as indicators of clinical peripheral nerve dysfunction.

Nerve conduction studies were done in all patients where a suitable nerve is selected so that it can be stimulated at two points along its course and the response was recorded by using surface electrodes placed over muscles supplied by that particular nerve. Following nerve conduction studies were performed to all patients on four limbs:

(Ulnar nerve, peroneal nerve, tibial nerve and sural nerve). In the motor nerve conduction study, the distal latency, amplitude of compound muscle action potential, conduction velocity and latency of F-waves were studied as evidence of peripheral neuropathy and in the sensory conduction study the latency and amplitude of sensory action potential were studied.

An elaborated clinical examination were performed in all patients with special reference to anemia, skin changes, peripheral nerve thickening, sensory and motor signs (especially ankle reflex). Supportive evidences like diagnostic ultrasound was taken as a diagnostic tool to assess the size of the kidney as kidneys are contracted in chronic kidney disease.

**Study assessment**

Measurement of total glomerular filtration rate is not possible; alternatively creatinine clearance test was followed to assess approximate values of total GFR even though it is a slight difference from the above.

Cockcroft-Gault equation:

$$\text{Estimated creatinine clearance (ml/min)} = \frac{(140 - \text{age}) \times \text{Body weight (kg)}}{72 \times \text{Plasma creatinine (mg/dl)}}$$

\*Multiply by 0.85 for women

Equation from the modification of diet in renal disease study

$$\text{Estimated GFR} = 1.86 \times (\text{Plasma creatinine})^{-1.154} \times (\text{age})^{-0.203}$$

\*Multiply by 0.742 for women.

**Statistical analysis**

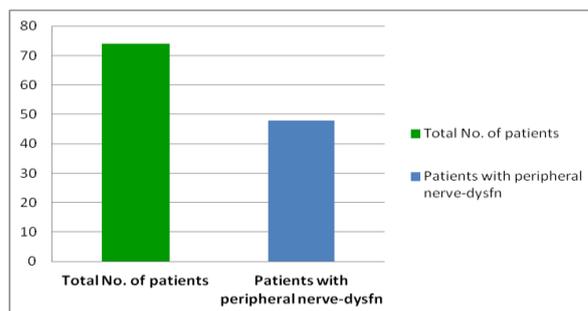
Values were expressed as mean. The prevalence of peripheral neuropathy and their type were analyzed by percentage difference.

**RESULTS**

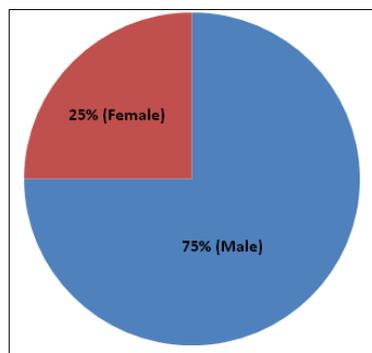
Total seventy four patients of different age groups with proved clinical, bio-chemical parameters in favor of chronic kidney disease were studied and different stages of CKD are shown in Table 1. The cross sectional study were shown that out of 74 patients, 48 patients (65 %) having peripheral nerve dysfunction (Figure 1) with the ratio of male and female (3:1) (Figure 2). However, we found peripheral nerves dysfunction was more affected with reference to age group (Figure 3). Moreover, the duration of disease increases the risk of peripheral nervous dysfunction as increase in more than 5 years of disease duration (Table 2). In comparison to sensory, the distal motor sensory neuropathy was the common type with chronic kidney disease (Table 3).

**Table 1: Different stages of chronic kidney disease.**

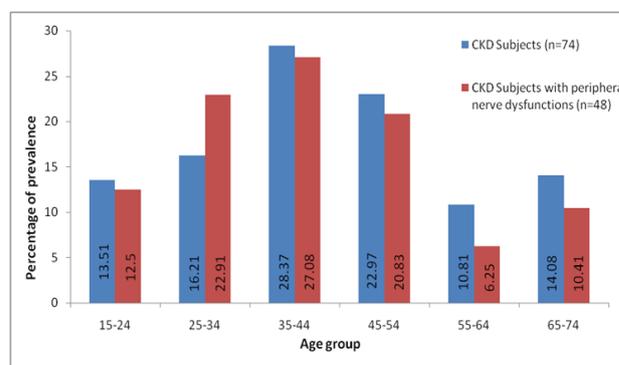
| Stage | Description                                    | GFR, ml/min per 1.73 m <sup>2</sup> |
|-------|--|-------------------------------------|
| 1.    | Kidney damage with normal GFR or increased GFR | ≥90                                 |
| 2.    | Kidney damage with mildly decreased GFR        | 60-89                               |
| 3.    | Kidney damage with moderately decreased GFR    | 30-59                               |
| 4.    | Kidney damage with severely decreased GFR      | 15-29                               |
| 5.    | End - stage renal disease                      | <15                                 |



**Figure 1: Percentage of prevalence of peripheral nerve dysfunction in study population (n=74).**



**Figure 2: Male and female ratio of prevalence peripheral nerve dysfunction among CKD patients (n=74).**



**Figure 3: Age specific prevalence of peripheral nerve dysfunction among CKD patients.**

**Table 2: The duration of the CKD increases as the prevalence of peripheral neuropathy increases.**

| Duration of chronic kidney disease | Total number of patients | Number patients with peripheral nerve dysfunction |
|------------------------------------|--------------------------|---|
| <1 years                           | 11                       | 4 (36%)   |
| 1-3 years                          | 21                       | 11 (52%)  |
| 3-5 years                          | 22                       | 16 (73%)  |
| >5 years                           | 20                       | 17 (85%)  |
| <b>Total</b>                       | <b>74</b>                | <b>48</b>   |

**Table 3: Electrodiagnostic study represents the presence of different types of peripheral neuropathy with the CKD patients.**

| Sensory motor | Sensory  | Motor    | Total    |
|---------------|----------|----------|----------|
| 25 (34%)      | 12 (16%) | 11 (15%) | 48 (65%) |

Interestingly, results shown that the males patients were affected more with the creatinine clearance <15 ml/mt, as observed patients affected with the creatinine clearance of <15 ml/mt were 72% and 67% of affected male and females, respectively. A 20% of affected males and 25% of affected females had a creatinine clearance of 15-29 ml/mt and both sexes were affected equally when the creatinine clearance is between 30-59 ml/mt (Table 4). The correlation in the prevalence of subclinical neuropathy is about 46% and overt neuropathy is 19 % (Table 5).

**Table 4: Creatinine clearance data of male and female patients having CKD.**

| Creatinine clearance (ml/min) | Total no. of patients (74) |             | Affected male (36) | Affected female (12) |
|-------------------------------|----------------------------|-------------|--------------------|----------------------|
|                               | M (53)                     | F (21)      |                    |                      |
| <15                           | 60%                        | 62%         | 72%                | 67%                  |
| 15-29                         | 31%                        | 8%          | 20%                | 25%                  |
| 30-59                         | 9%                         | 10%         | 8%                 | 8%                   |
| <b>Total</b>                  | <b>100%</b>                | <b>100%</b> | <b>100%</b>        | <b>100%</b>          |

**Table 5: Correlation between the overt and subclinical neuropathy.**

| Overt neuropathy | Subclinical neuropathy | Total    |
|------------------|------------------------|----------|
| 14 (19%)         | 34 (46%)               | 48 (65%) |

**DISCUSSION**

Chronic Kidney Disease (CKD) is a long term condition caused by damage to kidney. There is no single cause of damage and it is usually irreversible and can lead to ill health. In some cases dialysis or transplantation may become necessary for survival of patients. Recently epidemiology of CKD has been studied in detail with the finding that it is more common than previously thought.<sup>15-17</sup> Peripheral neuropathy is a recognized

complication of renal failure. Distal symmetrical sensory motor neuropathy is the commonest type of peripheral neuropathy observed in patients with chronic kidney disease. There is predilection for male in the prevalence of peripheral neuropathy in CKD when creatinine clearance is <15 ml/minute. Among all 74 patients, 48 patients showed evidence of peripheral nerve dysfunction either clinically or electrophysiologically. Thirty-six male patients showed features of peripheral nerve dysfunction and 12 female patients had evidence of peripheral nerve dysfunction. The duration of chronic kidney disease varied from 3 months to 7 years. An 85% of patients were shown features of peripheral nerve dysfunction either clinically or electrophysiologically when duration of CKD is more than five years. This shows that there is a linear correlation between the prevalence of peripheral neuropathy and duration of CKD. Patients who were presented with end stage renal failure have creatinine clearance <15 ml/minute, the prevalence of peripheral nerve dysfunction was noted more in these patients than in patients in whom the creatinine clearance was between 15-30 ml/minute.

In this study the polyneuropathy was most frequent in patients with highest levels of blood urea, creatinine and lowest creatinine clearances. However the duration of severe renal insufficiency also appeared to influence the onset of polyneuropathy.

In this study we have observed that the reduced motor nerve conduction velocity and sensory nerve conduction velocity was markers of peripheral neuropathy. This study doesn't account F-waves and H-reflex since these are essential for root lesions. Among these 48 patients, 34 patients had evidence of peripheral neuropathy in electrodiagnostic study, 14 patients had clinical evidence of peripheral neuropathy. A total of 11 patients had both motor and sensory symptoms in the form of loss of ankle jerk, defective appreciation of vibration sense. This finding may be emphasized with earliest clinical sign of neuropathy that is loss of ankle jerk. Two patients had numbness of both lower limbs and one patient has distal muscle weakness of both lower limbs. So prevalence of overt neuropathy was 19% and subclinical neuropathy was 46%.

The common type of peripheral neuropathy observed in this study was distal symmetrical sensory motor peripheral neuropathy and prevalence of this type of sensory motor neuropathy was 34%. The prevalence of sensory neuropathy was 16% and motor neuropathy was 15%. The other types of neuropathies like mononeuropathy, truncal neuropathies and cranial neuropathies were not registered in our clinical study.

This study shows the prevalence and clinical presentation of peripheral nerve dysfunction in patients with CKD that causes peripheral neuropathy. The CKD is found to cause peripheral neuropathy in 65% of patients both (19%) overt and (46%) subclinical neuropathy of which distal

symmetrical sensory motor neuropathy is common and the prevalence of peripheral neuropathy was directly proportional to duration and severity of chronic kidney disease.

## CONCLUSION

Chronic Kidney Disease (CKD) is recognized as a major health problem. As numbers of CKD patients increase, primary care practitioners will be confronted with management of the complex medical problems unique to patients with chronic renal impairment. This study enlightens the prevalence and clinical presentation of peripheral nerve dysfunction in patients with chronic kidney disease.

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