

# Movement disorder spectrum in chronic kidney disease(ckd) with clinical and radiological differentiation between patients with parkinsonism in ckd and idiopathic parkinsons disease(ipd)

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Chronic kidney disease (CKD) is defined as kidney dysfunction with progressive decline in glomerular filtration rate 60% patients with CKD has neurological symptoms in different stages of disease. Movement disorders are often dominating neurological symptoms. Among them myoclonus, restless leg syndrome, parkinsonism, asterixis are common presentation. In our study, we have analyzed the movement disorder spectrum in 71 CKD patients

and 50 patients with idiopathic parkinsons disease (IPD). Parkinsonism and myoclonus were the most common movement disorder being present in 46.5% and 45% of the cases. Postural tremor (13%) and restless leg syndrome (10%) were present in minority of patients. Bradykinesia (100%), rigidity (82%), postural instability (79%) and rest tremor (18%) were also present in the subset of patient having parkinsonism. Pyramidal sign and gait disorder were frequent in CKD patient with parkinsonism and rest tremor is less common. Hypertension and diabetes mellitus are more common seen in parkinsonism patients with CKD than those without.

**Key Words:** *Chronic kidney disease; Hypertension; Parkinsonism disease.*

## INTRODUCTION

Chronic kidney disease (CKD) is defined as kidney dysfunction with progressive decline in glomerular filtration rate 60% patients with CKD has neurological symptoms in different stages of disease. Movement disorders are often dominating neurological symptoms. Among them myoclonus, restless leg syndrome, parkinsonism, asterixis are common presentation. In our study, we have analyzed the movement disorder spectrum in 71 CKD patients and 15 patients with idiopathic parkinsons disease (IPD). Parkinsonism and myoclonus were the most common movement disorder being present in 46.5% and 45% of the cases. Postural tremor (13%) and restless leg syndrome (10%) were present in minority of patients. Bradykinesia (100%), rigidity (82%), postural instability (79%) and rest tremor (18%) were also present in the subset of patient having parkinsonism. Pyramidal sign and gait disorder were frequent in CKD patient with parkinsonism and rest tremor is less common. Hypertension and diabetes mellitus are more common seen in parkinsonism patients with CKD than those without.

## METHODS

This study was a prospective cross-sectional observation study conducted at Nil Ratan Sircar Medical College and Hospital, a tertiary center in Kolkata. 71 patients with chronic kidney disease and movement disorder were included in this study. 50 patients of Parkinson disease were also taken for comparison. This study was approved by the Ethics Committee of Nil Ratan Sircar Hospital and throughout the study medical confidentiality was kept.

## INCLUSION CRITERIA

Patients having eGFR<60 ml/min/1.73m<sup>2</sup> for >3 months irrespective of aetiology and status of renal replacement therapy.

## EXCLUSION CRITERIA

Subject with diagnosed movement disorder before the diagnosis of chronic kidney disease.

Subjects on antipsychotic medications, substance abuse.

Subjects not willing to participate.

Subjects are selected by using inclusion criteria and obtaining informed written consent. CKD patients were sub classified by eGFR, by using Modification of Diet in Renal Disease Study (MDRD) equation. Detailed clinical history,

drug history, general examination and neurological examination were performed in all patients. Parkinsonism was diagnosed based on presence of 2 of the following 4 clinical features-rest tremor, rigidity, bradykinesia, loss of postural reflex. Parkinsonism severity was evaluated by using Unified Parkinson's disease rating scale (UPDRS score) Part III: clinician-scored monitored motor evaluation. Levodopa response was assessed after 3 months based on UPDRS score [5]. RLS was diagnosed by International Restless Legs Syndrome Study Group (IRLSSG) criteria [6]. Routine blood parameters are done which include serum urea (mg/dl), creatinine (mg/dl), Hemoglobin (g/dl), serum sodium (meq/L), serum potassium (meq/L), and serum glucose (mg/dl), serum calcium (mg/dl), serum phosphorus levels (mg/dl). Magnetic resonance imaging was performed on a 1.5. Tesla supra-conducting magnet using T2-weighted (TR/TE 2000-2500/30 to 60 milliseconds) sequences in the transverse orientation, T1-weighted images (TR/TE 600/30 milliseconds) in the sagittal plane. The scans were evaluated for white matter hyper intensity (WMH), atrophy, hydrocephalus [7]. Hydrocephalus was calculated based on Evan's index i.e maximal ventricular width divided by the largest biparietal distance between the inner tables of the skull  $\geq 0.3$  Cerebral atrophy was found by volumetric analysis [8]. Cases having parkinsonism were compared with Parkinson's disease with respect to clinical signs and symptoms, radiological features and response to levodopa after three months. Data were analyzed by SPSS 20.0.1 and Graph Pad Prism version 5.

## RESULTS

In our study 71 cases having chronic kidney disease and some form of movement disorder were included. All cases were from rural and urban areas of West Bengal. In our case cohort 25% were female and 75% were male (Figure 1). The age distribution of cases ranged from 17 to 78 with median and standard deviation being 59 and 11.32 respectively (Figure 2). Parkinsonism and myoclonus were the most common movement disorder being present in 46.5% and 45% of the cases (Figure 3). Postural tremor (13%) and restless leg syndrome (10%) were present in minority of patients. Among the subset of patients having parkinsonism bradykinesia was present in all the cases. Rigidity (82%), postural instability (79%) and rest tremor (18%) were also present in the subset of patient having parkinsonism (Figure 4). The mean eGFR was lowest in those having myoclonus ( $12 \pm 6.27$ ). It was  $18.3 \pm 7.25$  in those having parkinsonism and  $19 \pm 8.27$  in those having restless leg syndrome. A comparison of mean eGFR of cases having parkinsonism was made with UPDRS score at initial visit. It showed negative correlation but it was statistically significant (Figure 5).

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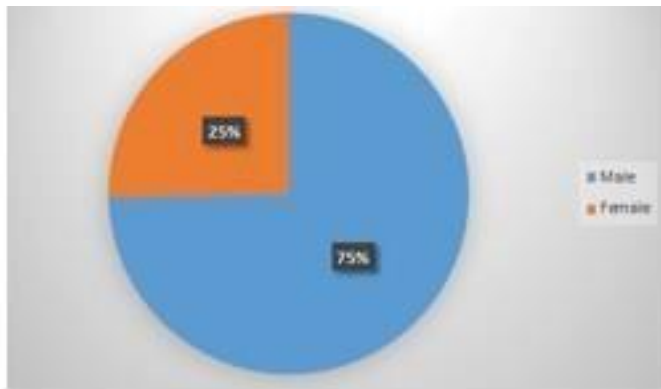


Figure 1: Sex distribution of Case Population.

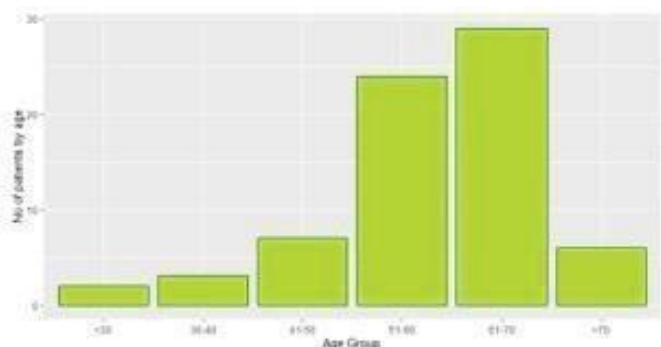


Figure 2: Age distribution of Case Population.

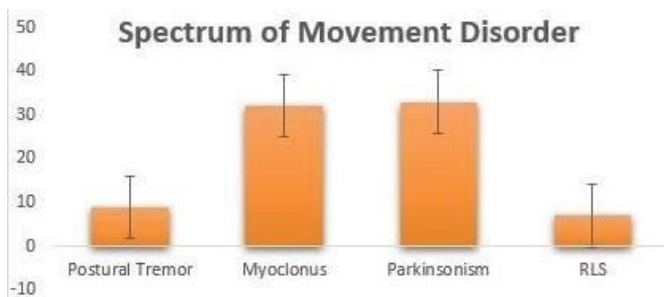


Figure 3: Movement disorder Spectrum in CKD.



Figure 4: Parkinsonian Features in CKD.

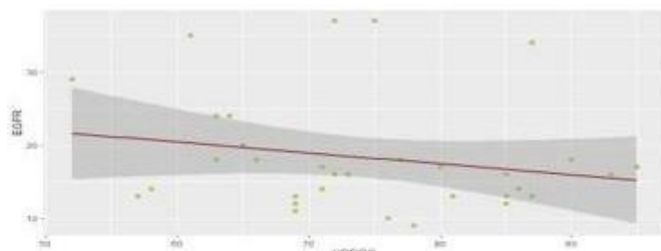


Figure 5: Scatter Plot Showing Correlation of Egrf and Updrs Score at Initial Evaluation of Cases Having Parkinsonism with Chronic Kidney Disease.

In the study we also compared the clinical and radiological features of parkinsonism patient having chronic kidney disease with those having

TABLE 1 Demographic and Clinical Characteristics at Baseline for the Patients in the Two Cohorts.

	Parkinsonism with Chronic Kidney Disease	Idiopathic Parkinson's Disease	p-value
Age	59.76	63.8	
Male	21(64%)	16(64%)	
Female	12(36%)	9(36%)	
Bradykinesia	33(100%)	25(100%)	0.2935
Rest Tremor	6(18%)	20(80%)	9.8E-06
Rigidity	27(82%)	18(72%)	0.5686
Pyramidal Sign	17(52%)	0(0%)	6.98E-05
Postural Instability	27(82%)	5(20%)	9.8E-06
Dysarthria	4(12%)	3(12%)	1
Urinary Abnormality	29(88%)	3(12%)	4.07E-08
Infarct	25(76%)	3(12%)	5.45E-06
White Matter Hyperintensity	25(76%)	3(12%)	5.45E-06
Normal	3(9%)	17(68%)	1.11E-05
Atrophy	13(39%)	7(28%)	0.5319
Hydrocephalus	2(6%)	0(0%)	0.5988

idiopathic Parkinson's Disease (Table 1). Both the cohort were matched for UPDRS score, mean age and sex ratio. Clinical features of both subset were significantly different. Rigidity, postural instability, pyramidal signs, urinary abnormality were more common among cases having parkinsonism with chronic kidney disease. Rest tremor was more common in those cases having idiopathic Parkinson's disease. Dysarthria was similarly present in both cohort. Radiological features were different among the two subset. Among the Idiopathic Parkinson's Disease cohort 68% had normal MRI features. Among those having abnormality diffuse atrophy was most common being present in 28% of cases. Lacunar infarct and white matter hyperintensity were both found in 12% of the above subset. In the of cohort of parkinsonism with chronic kidney disease MRI abnormality were present in 68% of cases. White matter hyperintensity and chronic infarct were most common being present in 76% cases of cohort. Rest of abnormality being diffuse atrophy and hydrocephalus. The response to levodopa therapy was different in both the groups. The mean UPDRS score of cases having idiopathic Parkinson's Disease decreased from 73.44 ± 7.33 to 52.44 ± 6.89 and those having parkinsonism with chronic kidney disease the decrement was less marked. It decreased from 74.18 ± 11.0 to 71.27 ± 10.88. The difference was statistically significant with p value being <0.005.

DISCUSSION

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. Glomerular filtration rate (GFR) is one component of excretory function, but is widely accepted as the best overall index of kidney function because it is generally reduced after widespread structural damage and most kidney functions decline in parallel with GFR in CKD. The normal GFR in young adults is approximately 125 ml/min/1.73m<sup>2</sup>. KDIGO 2012 guidelines has chosen a threshold of GFR <60ml/min/1.73 m<sup>2</sup> for >3 months to indicate CKD which is in concordance with previous KDOQI 2000 guidelines [9]. KDOQI recommended use of estimates of GFR calculated from prediction equations based on serum creatinine called as eGFR. In 1976, Cockcroft and Gault published an equation to predict creatinine clearance based on age, weight, height and plasma creatinine, together with correction factors [10]. Other equations commonly used are MDRD and CKD-EPI equations, each have its pros and cons [11].

Approximately 60% of patients with severe CKD, has neurological complications affecting central as well as peripheral system causing weakness, prolonged disability and alteration of mental state [4]. Asterixis, multifocal myoclonus and restless leg syndrome are most common movement disorders with parkinsonism is less prevalent. Acute parkinsonism, which is often reversible, seen most commonly in diabetic population of asian origin [2].

## Movement disorder spectrum in chronic kidney disease(ckd) with clinical and radiological differentiation between patients with parkinsonism in ckd and idiopathic parkinsons disease(ipd)

In our study we have found myoclonus (45%), parkinsonism (46.5%), rest tremor (18%), postural tremor (13%) and restless leg syndrome (10%). Parkinsonism and myoclonus are being most common. Chadwick in 1979 reported myoclonus occurred in patients with renal failure which was clinically similar to the action or intention myoclonus described by Wolfhart and Hook (1951) and Lance and Adams (1963) in syndromes of different aetiology [12]. Chorea is seen in patients with ESRD undergoing dialysis having thiamine deficiency, which was first described by Hung et al in 2001 [3]. Patients with ESRD have 1.55 times higher risk of developing PD than the control cohort. Asterixis or "flapping tremor" is caused from cortical dysfunction resulting in sudden loss of tonus and clinically consists of multifocal action-induced jerks [14]. In uremia, both spontaneous action myoclonus and stimulus-sensitive myoclonus with good response to benzodiazepines can occur. A typical movement disorder in uremic encephalopathy is the uremic "twitch-convulsive" syndrome that consists of intense asterixis and myoclonic jerks that are accompanied by fasciculations, muscle twitches and seizures. The most common extra pyramidal symptoms was gait disturbance (76%), followed by dysarthria (71%) and bradykinesia (47%). The 'typical' Parkinsonian features of tremor and rigidity (present in only 19% and 38%, respectively) were less prominent. In our study bradykinesia was present in all the cases with parkinsonism. Rigidity (82%), postural instability (79%) and rest tremor (18%) were also present in the subset of patient having parkinsonism. In CKD uremia may cause basal ganglia injury [15]. We found significant negative correlation between mean eGFR and UPDRS score at initial visit in patients with parkinsonism. In our study we found rigidity, postural instability, pyramidal signs, urinary abnormality were more common among cases having parkinsonism with chronic kidney disease and rest tremor was more common in IPD.

In the of cohort of parkinsonism with chronic kidney disease MRI abnormality were present in 68% of cases, with white matter hyperintensity and chronic infarct were most common, present in 76% cases. Greenamyre and Hastings have proposed that abnormal protein processing, oxidative stress, mitochondrial dysfunction, and inflammation play an important role in the pathogenesis of PD. Restless legs syndrome (RLS), was first described by K. A. Ekbom in 1944. In CKD patients the prevalence of RLS is 13.3% to 28% [13]. In our study 10% cases had RLS. It has been postulated that anemia and iron deficiency along with dopaminergic pathway dysfunction contribute to RLS [16].

### CONCLUSION

Wide spectrum of movement disorders are seen in patients with chronic kidney disease. It spans from cortical disorder like myoclonus to basal ganglia disorder like parkinsonism. Pyramidal sign and gait disorder were frequent in CKD patient with parkinsonism and rest tremor is less common. Hypertension and diabetes mellitus are more common seen in parkinsonism patients with CKD than those without. White matter hyperintensity in brain imaging is more common in CKD patients being most common. Parkinsonism symptoms in CKD patients are usually less responsive to levodopa therapy.

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Nil

### CONFLICTS OF INTEREST

There is no conflict of interest.

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