



## TO ASSESS SUBCLINICAL UREMIC ENCEPHALOPATHY IN NEWLY DIAGNOSED CHRONIC KIDNEY DISEASE PATIENTS BY USING ELECTROENCEPHALOGRAPHY IN TERTIARY CARE CENTRE

**Dr. Shubham Garg**

Post Graduate Student (MD), Department of Medicine, MGM College and MY Hospital Indore, MP, India

**Dr. Yogendra Jamra**

MD Medicine, Associate Professor, Department of Medicine, MGM College and MY Hospital Indore, MP, India

**Dr. Monika Porwal(Bagul)**

DNB Neurology, Assistant Professor, Department of Medicine, MGM Medical College and MY Hospital Indore, MP India.

**Dr. Sabiya Abdullah\***

Resident, Department of Medicine, MGM College and MY Hospital Indore, MP, India, \*Corresponding Author

### ABSTRACT

**Background:** Chronic kidney disease (CKD) is one of the leading cause of death in the world because of its late or end stage presentation. In our study we assessed patients of CKD for cognitive dysfunction with EEG (electroencephalography) and other biochemical parameters. **Methods:** This cross-sectional study was conducted on 60 newly diagnosed CKD patients at MGM Medical College and MY Hospital Indore, MP, India, from 2019 to 2021. Baseline parameters like serum urea, creatinine, bilirubin and sodium were done and patients were subjected to electroencephalography to assess subclinical uremic encephalopathy and data were analysed using SPSS statistics version 22.0 and p value <0.05 and confidence interval more than 95% were considered significant. **Results:** In this study, beta waves were found to be maximum in stage 1 (83.3%) whereas delta waves were found to be more in stage 5 (68%). In CKD stage 1, 16.7% patients had alpha waves and delta waves were absent. In CKD stage 5, 12% & 20% patients were having beta and alpha waves respectively. Epileptiform discharges were absent in patients of CKD stage 1 with stage 5 CKD having 80% patients with epileptiform discharges (P value =0.001). All patients in CKD stage 1 have symmetrical EEG waves, with 80% asymmetrical waves were present in CKD stage 5 (P value=0.021). **Conclusions:** This study supports the fact that as CKD stages progresses, there is propensity of delta waves, asymmetrical waves and epileptiform discharges which helps in early detection of subclinical uremic encephalopathy and therefore the risk of uremic seizures.

**KEYWORDS :** Chronic Kidney Disease, Delta Waves, Subclinical Encephalopathy.

### INTRODUCTION

There is increased risk for developing cognitive impairment in patients with Chronic kidney disease (CKD) as compared to the general population<sup>1</sup>. It is associated with albuminuria and low glomerular filtration rate in the patients of CKD<sup>2</sup>. The main pathology being cerebrovascular disease, also impaired clearance of urea, depression, sleep disturbance, anaemia, and different drugs could also be some contributory factors<sup>3</sup>. Clinical uremic encephalopathy due to renal failure can present with subtle symptoms of mental slowing, drowsiness, decreased mental acuity and vigilance to non-specific symptoms such as nausea, anorexia, restlessness, itching, and hypothermia to more obvious and grave symptoms such as seizures, myoclonus and even coma<sup>4</sup>. EEG not only provide us with a useful tool in assessing and monitoring progression of patients in uremic encephalopathy but also helps us to rule out structural brain disease and infections of central nervous system in CKD patients presenting with neurological symptoms and sign<sup>5</sup>. A timely recognition and prompt intervention can decrease the burden of morbidity caused by CKD. The clinical manifestations in patients of CKD having uremic encephalopathy vary from mild confusion to deep coma. They can also have movement disorders and clinically we can diagnose encephalopathy by asterixis<sup>6</sup>. Uremic encephalopathy is a major indication of dialysis (renal replacement therapy) with or without transplantation<sup>6</sup>. Uremic encephalopathy is generally reversible and usually takes 2-3 days before mental state clears, although some amount of mental deficit can still remain even after dialysis in patients with chronic renal failure. In case patient's alertness does not improve even after dialysis, it should raise the suspicion of some other etiology of encephalopathy. In most cases of dialysis disequilibrium syndrome, neurologic recovery is rapid and complete.<sup>7-10</sup>

### MATERIAL AND METHODS

This cross-sectional study is conducted on 60 newly diagnosed chronic kidney disease admitted in Medicine Department MGM Medical College and M.Y. Hospital, Indore to assess subclinical uremic encephalopathy in such patients from July 2019- February 2021.

### METHODOLOGY

The patient and/or his/ her legally acceptable representative were explained about the study in detail including the procedures, risks/benefits, etc. After obtaining their verbal approval for participation in the study, a voluntary written informed consent was obtained from them for participation in the study. All the study related procedures were carried out after obtaining the consent.

Sub-clinical uremic encephalopathy is defined in our study as patients with urea more than 100mg/dl, normal higher mental functions but with an abnormal EEG pattern in terms of delta waves, epileptiform discharges or symmetrical waves. A detailed medical history including the presenting complaints, history of any chronic medical illness, surgical history, history of drug treatment, family history of chronic medical illness or any familial surgical history were obtained. The personal history included diet, sleep, bowel, and bladder patterns. The patient underwent general and systemic examinations. Following which blood samples were collected for routine laboratory investigations and EEG was done on these patients.

### Ethical Considerations

This study was approved by the institutional ethical committee and review board. (EC/MGM/JAN-21/28.)

### Statistical Analysis

The data were initially entered into the Microsoft Excel for analysis. Online statistical software such as SPSS and

EpiInfo.Were used for calculating the values. Comparison of means between the groups was done using unpaired "t"-test and within the group was done using Paired "t"-test. Association between two non-parametric variables was done using the Pearson Chi-square test. P<0.05 was taken as statistically significant. The final data were presented in the form of tables and graphs.

**RESULTS**

As shown in table 1 and graph 1, CKD stage 1 had 16.7% of alpha waves and 83.3% of beta waves with no delta waves. In CKD stage 2, 33.3% patients had alpha waves, 50% patients had beta waves and 16.7% patients had delta waves. CKD stage 3 had 25% patients with alpha waves, 62.5% patients with beta waves and 12.5% with delta waves. CKD stage 4 had 33.3% alpha waves, 46.7% beta waves and 20% patients had delta waves. In CKD stage 5, 20% patients had alpha waves, 12% patients had beta waves and 68% patients had delta waves.

As shown in table 2 and graph 2, 100% of patient of CKD stage 1 having no epileptiform discharges. Compared to stage 1, stage 5 CKD has around 80% of patients with epileptiform discharges. Stage 4 has 46.66% patients with no epileptiform discharges while 53.33% has epileptiform discharges in stage 3. In CKD stage 2, 16.7% had epileptiform discharges.

In graph 3 and table 3, 100% of patients in CKD stage 1 having symmetrical EEG waves. While in CKD stage 5 we have 80% of patient with asymmetrical waves. In stage 4, 60% patients have asymmetrical waves while in stage 3 only 25% patients have asymmetrical wave. In CKD stage 2 we have 84% of symmetrical while rest (16%) asymmetrical.

**DISCUSSION**

Study concluded that, out of all 60 patients, 32 (53%) patients had asymmetrical EEG discharges while 28 (47%) patients out of 60 had symmetrical discharges.

In Stage 1 CKD we have 100% of symmetrical waves in EEG. In CKD stage 2 we have 84% of symmetrical waves while rest (16%) were asymmetrical. In CKD stage 3 we have 75% of symmetrical and 25% of asymmetrical waves. In CKD stage 4 we have 40% of symmetrical and 60% of asymmetrical waves. In CKD stage 5 we have 20% of symmetrical and 80 % of asymmetrical wave.

Swelman and Abdallah et al in a prospective observational study included 54 patients (22 males and 32 females) with different stages of chronic renal diseases.

Regarding symmetry of waves, 33 cases (61.1%) were symmetrical, 12(22.2%) were asymmetrical and 9 cases (16.7%) were dysrhythmic.<sup>11</sup>

Gadewar Acharyas et al 2015 stated any correlation of EEG in CKD. According to this study in stage 1 CKD they have all 100% waves asymmetrical compared to 75% in stage 2, 46.67% in stage 3, 26.67% in stage 4 and lowest in stage 5 which is about 15.38%. Conclusion of their study being, as stage progresses EEG waves tend to be more asymmetrical<sup>4</sup>.

Samir Tamer Abd- Allah, Doaa Mohammed Mahrous stated in their study regarding symmetry of EEG waves indifferent stages of CKD in which we can see that in stage 1 CKD 100% of symmetrical waves are found compared to 66.7% of symmetrical wave in stage 2 CKD. In stage 3 CKD we have equal percentage (33.3%) of symmetrical, asymmetrical and dysrhythmic waves<sup>12</sup>.

In my study in CKD stage 1 we have 16.7% of alpha waves and no patient with delta waves compared to 33.3% patients with alpha wave and 16.7% delta waves in stage 2. In stage 3 CKD

we have 25% of alpha waves, 62.5% of beta waves. In stage 4 we have 33.3% of alpha waves compared to 46.7% of beta wave, & 20% of delta waves. In CKD stage 5 we have 20% of alpha waves compared to 12% of beta waves and 68% of delta waves.

In contrast to our study, Gadewar Acharya et al 2015 shows, CKD stage 1 we have 100% of alpha waves compared to 68.75% in stage 2. In stage 3 CKD we have 56.25% of alpha waves, 12.5% of beta waves. In stage 4 we have 28.57% of alpha waves compared to 21.43% of beta wave, & 14.29% of delta waves<sup>4</sup>. In CKD stage 5 we have 38.46% of alpha waves compared to 15.38% of beta waves and 11.54% of delta waves. This trend shows the relation of increase in delta waves as the CKD stage progresses<sup>4</sup>.

Samir Tamer Abd- Allah, Doaa Mohammed Mahrous stated that 100% of waves in CKD stage 1 and stage 2 were alpha waves. In CKD stage 3 and 4 we have 66.7% were alpha waves whereas 33.3% were theta waves. In CKD stage 5 50% were alpha waves and 50% were theta waves<sup>12</sup>

In this study of 60 patients In CKD stage 1, 100% of patients had no epileptiform discharges, In CKD stage 2, 16.7% had epileptiform discharges. In CKD stage 3, 12.5% had epileptiform discharges. In CKD stage 4 53.3% patients had epileptiform discharges. In CKD stage 5, 80% patients had epileptiform discharges.

**Acknowledgements**

The authors would like to thank the teaching faculty, seniors and colleagues especially Dr. Sabiya and Dr. Umesh Chandra Sir in the department of Medicine, M.G.M. Medical College & MY Hospital Indore (MP).

**Conflict of interest – None**

**Ethical statement** - This study was approved by the institutional ethical committee and review board. (CODE: EC/MGM/JAN-21/28.)

**Table 1: Types of EEG waveforms in different stages of CKD.**

		CKD Stage					p
		STAG E 1	STAG E2	STAG E3	STAG E4	STAG E5	
WAV EFOR M	Alpha	Count 1	2	2	5	5	0.002
		% 16.7%	33.3%	25.0%	33.3%	20.0%	
	Beta	Count 5	3	5	7	3	
		% 83.3%	50.0%	62.5%	46.7%	12.0%	
	delta	Count 0	1	1	3	17	
		% 0.0%	16.7%	12.5%	20.0%	68.0%	
Chi Square test- P=0.002 significant							

**Table 2: CKD stages and percentage of epileptiform discharges**

		EEG (EPILEPTIFORM DISCHARGE)		p
		no	yes	
CKD Stage	STAGE 1	Count 6	0	<0.001
		% 100%	0.0%	
	STAGE 2	Count 5	1	
		% 83.3%	16.7%	
	STAGE 3	Count 7	1	
		% 87.5%	12.5%	
STAGE 4	Count 7	8		
	% 46.66%	53.33%		
STAGE 5	Count 5	20		
Chi Square test- P=0.001 significant				

**Table 3 – CKD stages and background of the waves.**

EEG(BACKGROUND)		P
Asymmetrical	Symmetry	

CKD Stage	STAGE 1	0	6	<0.001
		0.0%	100%	
	STAGE 2	1	5	
		16.7%	83.3%	
	STAGE 3	2	6	
		25%	75%	
	STAGE 4	9	6	
		60%	40%	
	STAGE 5	20	5	
		80%	20%	

Chi Square test- P=0.001 significant

Types of EEG waveforms in different stages of CKD

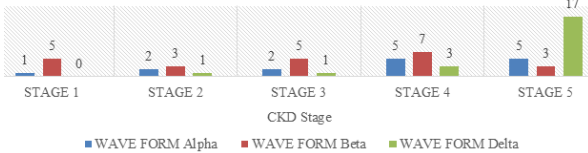


Figure 1

CKD stages and percentage of epileptiform discharges

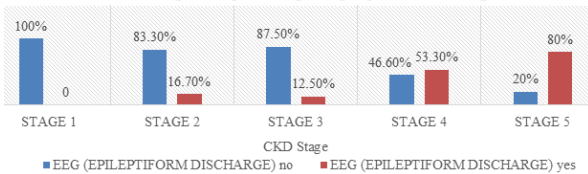


Figure 2:

CKD stages and background of the waves

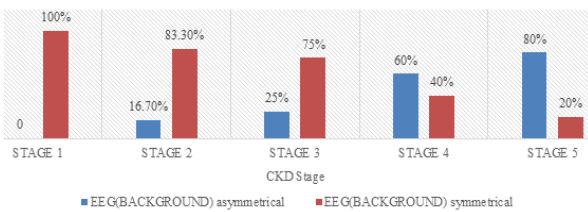


Figure 3

REFERENCES

1. Bronas UG, Puzantian H and Hannan M. Cognitive Impairment in Chronic Kidney Disease: Vascular Milieu and the Potential Therapeutic Role of Exercise. *Biomed Res Int.* 2017;2017:2726369.
2. Levey AS, Becker C and Inker LA. Glomerular filtration rate and albuminuria for detection and staging of acute and chronic kidney disease in adults: a systematic review. *JAMA.* 2015; 313: 8:837-846.
3. Drew DA, Weiner DE and Sarnak MJ. Cognitive Impairment in CKD: Pathophysiology, Management, and Prevention. *Am J Kidney Dis.* 2019; 74:6:782-790.
4. Gadewar P, Acharya S, Khairkar P, Shukla S, Mahajan SN. Dynamics of electroencephalogram (EEG) in different stages of chronic kidney disease. *J Clin Diagn Res.* 2015;9(3):OC25-OC27.
5. mmady PD, Anilkumar AC. EEG Abnormal Waveforms. [Updated 2021 Jul 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557655/>
6. Seifter JL, Samuels MA. Uremic encephalopathy and other brain disorders associated with renal failure. *Semin Neurol.* 2011 Apr;31(2):139-43. doi: 10.1055/s-0031-1277984. Epub 2011 May 17..
7. Chen R, Young GB. Metabolic Encephalopathies. In: Baillere's Clinical Neurology, Bolton CF, Young GB (Eds), Bailliere Tindall, London P577.
8. Plum F, Posner JB. The Diagnosis of Stupor and Coma, FA Davis Company, Philadelphia 1982. P177.
9. Young GB, DeRubeis DA. Metabolic encephalopathies. In: Coma and Impaired Consciousness, Young GB, Ropper AH, Bolton CF (Eds), McGraw-Hill, 1998. P307.
10. Bolton CF, Young GB. Uremic encephalopathy. In: Neurological Complications of Renal Disease, Bolton CF, Young GB (Eds), Butterworths, 1990. P44.
11. Raja Purkar M, M john et al what do we know about chronic kidney disease in India: first report of Indian CKD registry. *BMC nephrol* 2012:13.
12. SalwaSwelam; Samir Abdallah; DoaaMahrousElectroencephalogram findings in chronic kidney disease. 2019;5:14:25-31.