

# ELECTROGRAPHIC SIGNIFICANCE OF PERIODIC DISCHARGES AND ASSOCIATION WITH ETIOLOGY AND OUTCOME IN A TERTIARY CARE HOSPITAL: A RETROSPECTIVE COHORT STUDY

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## ABSTRACT

### Background and Objective:

Periodic discharges on electroencephalograms (EEGs) are rhythmic waveforms that may indicate acute or subacute brain injury. This aim of this study was to determine the frequency distribution of periodic discharge subtypes on EEG and to assess their association with underlying etiologies and clinical outcomes in a tertiary care hospital.

### Methods:

This retrospective observational cohort study included neurological patients aged  $\geq 18$  years admitted to the medical ICU or ward of Aga Khan University Hospital between January 1, 2021, and January 1, 2023, with periodic discharges on EEG. Patients with prior traumatic brain injury were excluded. Data on demographics, clinical presentation, EEG subtype, neuroimaging findings, management, and outcomes were extracted from medical records. Statistical analysis was performed using SPSS version 22, with categorical variables presented as frequencies and percentages, continuous variables as mean  $\pm$  standard deviation, and significance set at  $p \leq 0.05$ .

### Results:

Out of 41 patients, 51.2% were female, with a mean age of 58.5 years. Generalized tonic-clonic seizures were the most common presentation (48.8%), and ischemic stroke was the leading etiology (31.7%). Lateralized periodic discharges were the most frequent EEG subtype. Chronic imaging changes were present in 34%, most often encephalomalacia and gliosis. Most patients (87.8%) were discharged home, while mortality occurred in 12.2%, often linked to status epilepticus or metabolic encephalopathy.

### Conclusion:

Periodic discharge subtypes, particularly lateralized patterns, are often associated with ischemic stroke and severe neurological presentations. Their recognition and etiological correlation are essential for timely intervention and improved patient outcomes.

**Keywords:** Electroencephalogram, Encephalopathy, Lateralized, Periodic discharges, Seizures, Stroke.

## INTRODUCTION

Periodic discharges are waves or complexes that occur most of the time at regular or near regular interval. These may last for up to several seconds. The description of the term “periodicity” was formally upgraded in 2005, when the American Clinical Neurophysiology Society explained it as the recurrence of waves that were similar in structure and duration plus had a measurable interval in between two successive waves, almost the same between any two waves following each other.<sup>1</sup> Lateralization as described by Chatrian

in 1964, points out the focus of discharges on electroencephalogram (EEG) originating from one cerebral hemisphere.<sup>2</sup>

However, the umbrella of periodic discharges also includes generalized periodic discharges (GPDs), bilateral independent periodic discharges (BIPDs), and even triphasic waves. The fact that some of these discharges may not be clearly epileptogenic emphasizes the significance of recognition of various patterns of periodic discharges.

Thus, the causative disease processes behind the findings of lateralized periodic discharges (LPDs) on EEG ranges from cerebral infarction to infection like herpes simplex virus (HSV) and prion-related Creutzfeldt Jakob disease (CJD), from fast growing tumors to subacute pathologies like demyelination, from new onset seizures to chronic epilepsy syndromes and rarely from anoxic injury in critically ill patients to those with toxic or metabolic encephalopathies.

The objective of this study was to determine the frequency of various subtypes of periodic discharges on EEGs done in patients during the defined study period and co-relate with etiology and clinical outcome of the patient.

## METHODS

This retrospective observational cohort study was conducted over two years from January 1st, 2021, to January 1st, 2023, at Aga Khan University Hospital in Karachi. All patients fulfilling the inclusion criteria during the study period were included in the study. The inclusion criteria encompassed individuals aged 18 years and above, admitted in either medical intensive care unit (ICU) or ward during the study period, showing periodic discharges. Notably, patients with a history of traumatic brain injury were excluded from the study.

The study received approval from the Departmental Research Committee, and data collection was carried out by

the primary investigators. All information was obtained from the patients' medical records as per the designed proforma which comprised of the variables as age, gender, comorbid conditions, management, admission to ICU and ward, symptoms, mortality, and treatment. EEGs were read and reported by trained neurologists.

SPSS version 22 was used for data analysis. Frequency and percentages were computed for categorical variables like gender, symptoms at onset (seizures, altered level of consciousness, stroke), EEG findings (LPDs, BIPDs, GPDs, triphasic waves), etiologies (status epilepticus, stroke, infection, brain tumor, toxic or metabolic encephalopathy), number of anti-epileptics received, and functional outcomes using modified rankin scale (mRS). Values were presented as mean  $\pm$  standard deviation for continuous variables like age. P values equal to or less than 0.05 were considered significant.

## RESULTS

A total of 41 patients underwent electroencephalography for various diagnostic and therapeutic indications, most commonly in the ward, followed by the intensive care unit, and in a minority, the emergency department. Of these, 21 (51.2%) were female and 20 (48.8%) were male, with a mean age of 58.5 years. The most frequent clinical presentation was generalized tonic-clonic seizures, observed in 48.8% of patients (Table 1).

**Table 1:** Baseline Characteristics, EEG Findings, Etiologies, Treatments, and Outcomes of the Study Population.

Variables	n (%) / Mean $\pm$ SD
<b>Demographics</b>	
Age (years)	58.5 $\pm$ 17.6
Male	20 (48.8)
Female	21 (51.2)
<b>EEG Setting</b>	
Ward	26 (63.4)
ICU	13 (31.7)
Emergency	2 (4.9)
<b>Clinical Presentation</b>	
Generalized tonic–clonic seizures	20 (48.8)
Focal seizures	10 (24.4)
Altered level of consciousness	9 (22.0)
Focal neurological deficit	2 (4.9)
<b>EEG Findings</b>	
LPDs	24 (58.5)
BIPDs	7 (17.1)
GPDs	3 (7.3)
Triphasic waves	7 (17.1)
<b>Etiology</b>	
Status epilepticus	6 (14.6)
Acute ischemic stroke	13 (31.7)
Infection	9 (22.0)
Brain tumor	2 (4.9)
Metabolic/toxic encephalopathy	6 (14.6)
Hemorrhagic stroke	5 (12.2)
<b>Treatment</b>	
No ASM	1 (2.4)
Single ASM	17 (41.5)
Two ASMs	13 (31.7)
More than two ASMs	10 (24.4)

<b>Outcome</b>	
Discharged	36 (87.8)
Expired	5 (12.2)
<b>Fever on Presentation</b>	
Present	9 (22.0)
<b>Level of Consciousness at Presentation</b>	
Confused/disoriented	14 (34.1)
Drowsy	24 (58.5)
Stuporous	1 (2.4)
Comatose	2 (4.9)
<b>Findings on CT/MRI</b>	
Acute ischemic stroke	10 (24.4)
Hemorrhage	5 (12.2)
Tumor	2 (4.9)
Meningeal enhancement	8 (19.5)
Encephalomalacia/gliosis/old ischemic changes	14 (34.1)
Hydrocephalus	2 (4.9)
<b>Findings on Lumbar Puncture</b>	
Normal	8 (19.5)
Isolated raised protein	6 (14.6)
Infection with neutrophilic pleocytosis	2 (4.9)
Infection with lymphocytic pleocytosis	6 (14.6)
Not done	19 (46.3)
<b>Functional Status on Discharge (mRS)</b>	
mRS 1	5 (12.2)
mRS 2	6 (14.6)
mRS 3	8 (19.5)
mRS 4	12 (29.3)
mRS 5	5 (12.2)
mRS 6	5 (12.2)

ASM: Anti-seizure medication, BIPDs: Bilateral independent periodic discharges, CT: Computed tomography, EEG: electroencephalogram, GPDs: Generalized periodic discharges, ICU: intensive care unit, LPDs: Lateralized periodic discharges, MRI: Magnetic resonance imaging. mRS: Modified Rankin Scale

At presentation, the majority had an altered mental status. Fever was present in nine patients, attributable to either central nervous system or systemic infection. In suspected infective etiologies, slightly over half of the patients underwent lumbar puncture. Approximately one-third had normal cerebrospinal fluid (CSF) findings, while among abnormal results, isolated elevated protein or elevated protein with lymphocytic pleocytosis were the most common diagnostic clues.

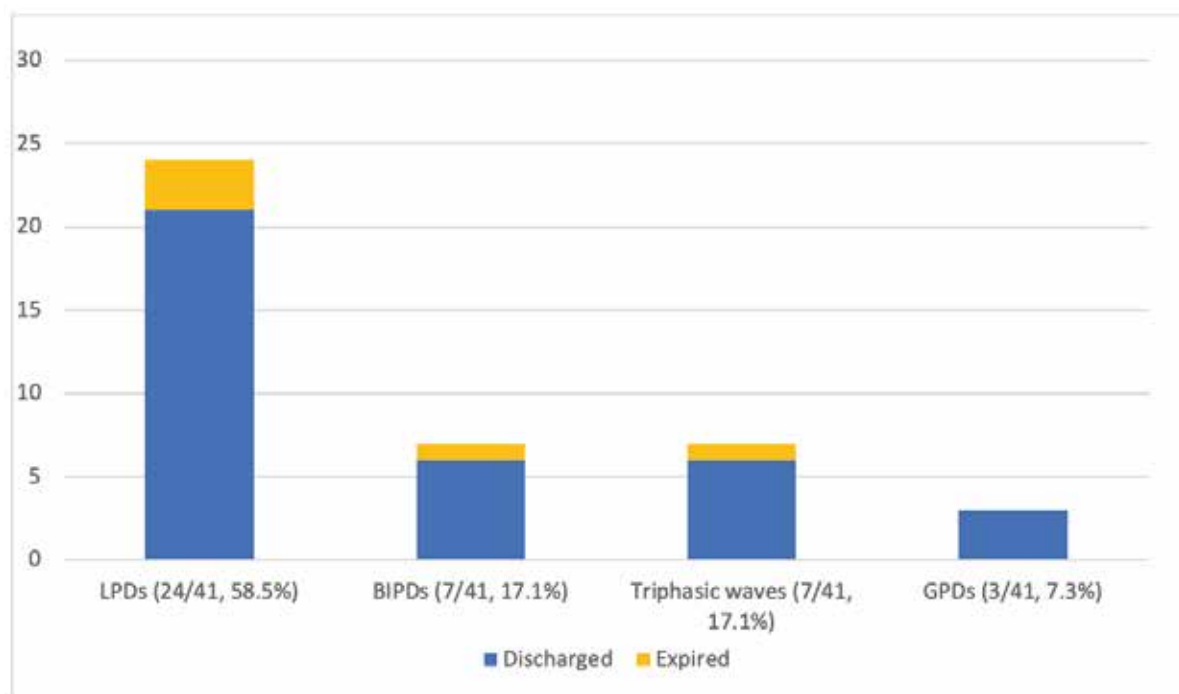
Nearly two-thirds of the cohort demonstrated LPDs on EEG. Etiologies for LPDs were multifactorial, most frequently ischemic stroke (31.7%), followed by central nervous system infections e.g. HSV (22%), status epilepticus (14.6%), metabolic/toxic encephalopathy (14.6%), hemorrhagic stroke (12.2%), and brain tumors (4.9%).

BIPDs and triphasic waves were the next most common EEG patterns, each occurring in 7% of patients. Generalized tonic-clonic seizures were the predominant presentation for both (48.8%), whereas focal seizures were rare. Patients with BIPDs or triphasic waves without seizures at onset typically presented with acute encephalopathy. In a minority of patients presenting with generalized seizures, focal seizures, or altered mentation

with or without neurological deficits, EEG revealed generalized periodic discharges.

All our subjects underwent neuroimaging, which revealed structural abnormalities in almost all the patients; findings were both acute and chronic. Encephalomalacia, gliosis, or old ischemic changes were the most common, observed in 34% of patients. Ischemic stroke was seen in 24.4% of cases, while meningeal enhancement was present in 19.5%.

Except for 2.4% who received no anti-seizure medications, most patients required a single drug, while 10% were managed with more than two agents based on clinical status. Thirty six percent of our patients were discharged home; however five patients (four females, one male) died (Table 2). Of these, three had LPDs, and one each had BIPDs and GPDs (Figure 1). Status epilepticus or metabolic encephalopathy was the primary etiology in four deaths, and stroke in one. Encephalomalacia or gliosis was present in three of the deceased. Regarding functional outcomes as shown in Table 3, 19 patients had an mRS  $\leq 3$ , and 22 had an mRS  $\geq 4$ , with the most common score being 4 (29.3%).



**Figure 1:** Distribution of EEG patterns among patients, stratified by outcome (discharged vs. expired). LPDs were most frequent (58.5%), followed by BIPDs (17.1%), triphasic waves (17.1%), and GPDs (7.3%).

**Table 2:** Comparison of demographic, clinical, EEG, radiological, and laboratory characteristics between discharged and expired patients.

<b>Age, years</b>	58.2 ± 17.8	60.8 ± 17.5	0.76
<b>Gender</b>			
Male	19 (52.8)	1 (20)	0.34
Female	17 (47.2)	4 (80)	
<b>EEG setting</b>			
Ward	26 (72.2)	2 (40)	0.30
ICU	10 (27.8)	3 (60)	
<b>Clinical presentation</b>			
Generalized tonic clonic	20 (55.6)	0	0.008
Focal seizure	9 (25)	1 (20)	
Altered level of consciousness	5 (13.9)	4 (80)	
Focal neurological deficit	2 (5.6)	0	
<b>EEG finding</b>			
LPDs	21 (58.3)	3 (60)	0.92
BIPDs	6 (16.7)	1 (20)	
GPDs	3 (8.3)	0	
Triphasic waves	6 (16.7)	1 (20)	
<b>Etiology</b>			
Status epilepticus/Metabolic	17 (47.2)	4 (80)	0.37
Stroke	17 (47.2)	1 (20)	
Brain Tumor	2 (5.6)	0	
<b>Treatment</b>			
No AED	1 (2.8)	0	0.61
Single AED	14 (38.9)	3 (60)	
Two or more AEDs	21 (58.3)	2 (40)	
<b>Consciousness on presentation</b>			
Confused/Disoriented	13 (36.1)	1 (20)	0.54
Drowsy	20 (55.6)	4 (80)	
Stuporous/Comatose	3 (8.3)	0	
<b>Findings on CT/MRI</b>			
Ischemic/Hemorrhage stroke	9 (31)	1 (25)	0.58
Meningeal enhancement	5 (17.2)	0	
Encephalomalacia/Glisis/Old ischemic changes	15 (51.7)	3 (75)	
<b>Findings on Lumbar Puncture</b>			
Normal	7 (19.4)	1 (20)	0.78
Isolated raised protein	6 (16.7)	0	
Infection with neutrophilic Pleocytosis	7 (19.4)	1 (20)	
Not done	16 (44.4)	3 (60)	

**Table 3:** Functional outcomes at discharge, measured by Modified Rankin Scale (mRS), across patients with LPDs, BiPDs, GPDs, and triphasic waves.

	LPDs n=24	BiPDs n=7	GPDs n=3	Triphasics n=7
mRS 1	4	-	-	1
mRS 2	6	-	-	-
mRS 3	5	1	-	2
mRS 4	4	4	1	3
mRS 5	2	1	2	-
mRS 6	3	1	-	1

## DISCUSSION

Periodic EEG patterns are not an uncommon finding seen in critically ill patients. They may be lateralized or generalized, signifying acute or subacute brain damage.<sup>3</sup> Such periodic discharges carry predisposition to occurrence of seizures, but are not necessarily epileptiform, and hence the nomenclature proposed by American Clinical Neurophysiology Society has been changing to better define the terminologies.<sup>1</sup>

The most extensively studied periodic EEG rhythm is known as lateralized periodic discharges.<sup>4</sup> In one study involving 3,436 patients, 24 individuals were found to have LPDs, with cerebrovascular occlusion being the most frequently identified cause, and 20 of these patients experienced seizures.<sup>5</sup> Our own study also observed a high prevalence of LPDs in almost two-thirds of the patients, with ischemic stroke being the most common etiological factor, aligning with the findings of this study. Although LPDs are classically linked to acute or subacute cortical lesions, the predominance of chronic changes in our cohort may reflect delayed presentation to our tertiary center or chronic lesions acting as epileptogenic substrates triggered by new systemic or neurological insults.

Additionally, bilateral independent periodic discharges and triphasic waves were equally common in our institution and were frequently associated with generalized tonic clonic seizures. The spectrum of clinical presentation is quite like that seen in previous literature, with majority of patients having generalized tonic clonic seizures. Those who do not fulfil the former criteria are bound to have other signs of neurological impairment, as depicted in a review conducted by Chatrian.<sup>2</sup>

In accordance with a descriptive study carried out by Khana et al, the nature of periodic discharges is reflective of extent of cortical or subcortical dysfunction and explains why lateralized periodic discharges were more common in focal pathologies like ischemic stroke, herpes encephalitis, head injury or intra-cranial hemorrhage, while bilateral independent periodic discharges or generalized periodic discharges were indicative of more diffuse cerebral damage.<sup>6</sup> In contrast, our study showed variability in association between etiology and type of periodic discharge.

Interestingly, 34% of our study population had chronic changes in the imaging, while amongst those who had

acute findings on the scans, ischemic stroke remained the most common etiology. A study by Lin L and colleagues on periodic EEG patterns seen in ICU established absence of structural lesions on neuroimaging of patients having LPDs in about 25-33%, even though periodic discharges with a lateralized pattern is a marker of cortical gray or subcortical gray and white matter injury.<sup>7</sup>

With regards to the outcome, 36 out of 41 patients enrolled in the study were discharged home. The outcome was closely related to the etiology and clinical course of the individual. Only 5% achieved independent living after discharge (mRS-1). Several studies have highlighted the prognostic implications of periodic discharges, with greater morbidity and mortality associated with generalized or bilateral independent periodic discharges compared to lateralized periodic discharges. This is consistent with our findings, where LPDs were the dominant pattern observed, and only 12% of our cohort succumbed to their illness.

In a study evaluating long-term outcomes of 39 individuals with LPDs, recent stroke accounted for 33% of cases, like our findings. However, that study reported a higher mortality rate of 41%, with 16 patients dying during hospitalization or within two months post-discharge.<sup>8</sup> In our study, five patients (12%) died, three with LPDs and one each with BIPDs and GPDs. In contrast, other studies have shown BIPDs to have higher mortality, with anoxic encephalopathy (28%) and CNS infections (28%) being predominant causes among BIPD cases.<sup>9,10</sup>

This study is limited by its small sample size, single-center setting, and retrospective design, which introduces selection bias and limits generalizability.

EEG monitoring was not standardized, and treatment decisions varied by clinician, potentially influencing outcomes. The absence of long-term follow-up restricts assessment of delayed mortality or recovery, and the heterogeneous etiologies in our cohort add potential confounding.

Despite our limitations, the findings of our retrospective cohort highlight the importance of comprehensively assessing periodic discharges in EEGs, particularly in tertiary care settings. By examining 41 patients, we demonstrate the diverse etiologies and clinical presentations associated with these discharges, ranging from ischemic stroke to infections and metabolic encephalopathies. These insights emphasize the need for a nuanced approach in diagnosis and management. Furthermore, correlating discharge subtypes with specific etiologies provides valuable clinical information that may guide treatment and improve patient prognosis.

## CONCLUSION

Periodic discharges on EEG represent a diverse group of patterns with varying etiologies and prognostic implications. In our cohort, LPDs were the most observed pattern, primarily linked to structural brain lesions. Compared to other periodic discharge patterns such as BIPIDs and GPDs, LPDs were associated with lower mortality rates. However, despite survival, a considerable proportion of patients experienced persistent functional dependence, highlighting the substantial impact of the underlying neurological condition and clinical trajectory on patient outcomes.



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Authors' contribution:

**Zainab Memon:** Concept, Data analysis and interpretation, manuscript writing

**Hina Imtiaz:** Design, data collection and analysis, manuscript writing

**Ayisha Farooq Khan:** Design, data analysis, manuscript revision

**Dureshahwar Kanwar:** Design, data interpretation, manuscript revision

**Safia Awan;** Data analysis, manuscript writing

All the authors have approved the final version to be published and agree to be accountable for all aspects of the work.



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