

Clinical and Radiological Profile of Post Stroke Seizures

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Abstract

In population studies, stroke is the most commonly identified cause of epilepsy in adult populations older than 35 years¹. In the elderly, stroke accounts for more than half of the newly diagnosed cases of epilepsy in which a cause is determined, ahead of degenerative disorders, brain tumors and head trauma¹. From stroke registry data, about 5% to 20% of all individuals who have stroke will have subsequent seizures.^{2,3} but epilepsy will develop in only a small subset of this group.

Materials and Methods

The present study was conducted in the Postgraduate Department of Medicine, Government Medical College, and Srinagar. A total of 104 patients admitted to the Department of Medicine, SMHS Hospital with post stroke seizures were enrolled in the study from December, 2017 to December, 2019. Our study was an observational one.

Introduction

Stroke is the second leading cause of death globally being responsible for five and a half million deaths annually.¹ It is associated with high degree of morbidity and is a well-recognized cause of symptomatic epilepsy in adults. Stroke increases the risk of seizures and

epilepsy at any age but is the most among cause of seizures in the elderly². The incidence of seizures after stroke has been reported to varying range from 2% to 67%.^{3,4} The overall rate of post ischemic seizures is 2-4%.⁴ Like stroke, post-stroke seizures are also more prevalent in the population over 65 years of age and can occur after any type of stroke. It can be a sole manifestation of a new cerebrovascular event or may present in either early or late phase after stroke. Male gender, age greater than 65 years, anterior circulation infarction cortical location and large lesion are the factors associated with post-stroke seizures.^{5,6} Other reported factors include haemorrhagic infarcts, cerebral venous infarcts and stroke recurrence. International data show preponderance of early seizures, majority presenting with focal seizures especially in young adults.⁷ The early seizure is thought to be associated with a high risk of status epilepticus and an increased death rate.⁸ The highest rate of late seizure is in the first year after stroke and is related to high likelihood of developing post stroke epilepsy.⁷ The impact of post-stroke seizures on functional outcome and mortality remains a debate especially in early seizures.⁹ Bladin et al¹¹ found the incidence of seizures to be 10.6% among 265 patients with intracerebral

hemorrhage versus 8.6% among 1632 with ischemic stroke. In another prospective series,¹³ seizures occurred in 4.4% of 1000 patients, including 15.4% with lobar or extensive intracerebral hemorrhage, 8.5% with subarachnoid hemorrhage, 6.5% with cortical infarction, and 3.7% with hemispheric transient ischemic attacks. A seizure was presenting feature of intracranial hemorrhage in 30% of 1402 patients.¹¹ Among 95 patients with aneurysmal subarachnoid hemorrhage, the incidence rate of prehospital seizures was higher (17.9%) than that occurring in the hospital (4.1%)¹⁴.

Post-stroke seizures typically follow a localisation related (focal) seizure semiology, but about one third of cases present with tonic-clonic (generalised) seizures and the remaining two thirds usually present with partial seizures. Early onset seizures usually present with a focal onset while generalised tonic-clonic seizures are more common with late onset seizures. It is worthwhile remembering that there are atypical presentations of post-stroke seizures as well as seizure mimics; both of which can give rise to confusion and subsequent delay in appropriate diagnosis and management. Status epilepticus develops in 9% of cases. Although the immediate prognosis of patients with status epilepticus is poor, status epilepticus as a presentation does not predict subsequent development of epilepsy.¹⁹ The independent effect of status epilepticus on mortality outcome is controversial.^{19,20,21} The type of stroke, topographic findings, size of the lesion, or electroencephalographic (EEG) pattern do not predict the progression to status epilepticus.²²

Seizures after stroke are classified as early or late onset, according to their timing after brain Ischemia, in a paradigm comparable to post-traumatic epilepsy^{11,16}. An arbitrary cut point of two weeks after the present-

day stroke has been recognized to distinguish between early and late onset post-stroke seizures^{15,17,18}. Different characteristics and mechanisms of post-stroke seizures according to their proximity to the onset of brain-ischemia have been composed, but no clear pathophysiological basis exists for the two week cut point. Most early onset seizures occur during the first 1-2 days after ischemia. In a series restricted to early-onset seizures, 90% of the 30 patients had ictal activity within the first 24 hours. Most seizures associated with hemorrhagic stroke also occur at onset or within first 24-hours²³.

During acute-ischemic injury, accumulation of intracellular calcium and sodium may result in depolarization of the transmembrane potential and other calcium mediated effects. These local ionic shifts may lower the seizure threshold^{11,24}. Glutamate excitotoxicity is a well-established mechanism of cell death in the experimental stroke model. Antiglutaminergic drugs may also have a neuroprotective role in ischemic settings, aside from the role of treating seizures.

The size of regional metabolic dysfunction may also be relevant in causing early-onset seizures. In the setting of large regions of ischemic hypoxia, high levels of excitotoxic neurotransmitters may be released extracellularly. In the studies of post-ischemic brain in experimental animal models, neuronal populations in the neocortex²⁵ and hippocampus²⁶ have altered membrane properties and increased excitability, which presumably lower the threshold for seizure initiation. The ischemic penumbra, a region of viable brain tissue adjacent to the infarcted core in ischemic stroke, contains electrically irritable tissue that may be a focus for seizure activity.

In addition to focal ischemia, global hypoperfusion can

cause seizure activity. Hypoxic-ischemic encephalopathy is one of the most common causes of status epilepticus and carries a poor prognosis. Particularly vulnerable to ischemic insult is the hippocampus, which is an especially epileptogenic area. In late-onset seizures, by contrast, persistent changes in neuronal excitability occur. Replacement of healthy cell parenchyma by neuroglia and immune cells may play a role in maintaining these changes. A gliotic scarring has been implicated as the nidus for late-onset post-traumatic epilepsy¹¹.

An underlying permanent lesion appears to explain the higher frequency of epilepsy in patients with late-than-early-onset seizures. As in post-traumatic epilepsy²⁷, late occurrence of a first seizure appears to carry a higher risk for epilepsy.

The present study was planned to know the:

1. Clinical features of post stroke seizures with special reference to
 - a. Time of onset –
 - Early (< 2 weeks)
 - Late (>2 weeks)
 - b) The type of seizure
 - i. Generalized
 - ii. Partial with secondary generalization
 - iii. Partial
 - c) Frequency
 - i) Single
 - ii) Multiple
 - d) Status epilepticus
 - a) Yes
 - b) No
2. The radiological characteristics on CT / MRI
 - Type of stroke

- i) Ischemic
 - a) Arterial (lacunar or large vessel)
 - b) Venous
- ii) ICH
 - Location
 - a) Cortical
 - b) Subcortical

The present study was conducted in the Postgraduate Department of Medicine, Government Medical College, and Srinagar. Patients admitted to the Department of Medicine, SMHS Hospital with post stroke seizures were enrolled in the study from December, 2017 to December, 2019.

Inclusion and Exclusion Criteria

Inclusion Criteria: All the adult patients over the age of 20 years, from both the genders admitted to Government Medical College diagnosed as post stroke seizures from December, 2017 to December, 2019 were included in the study.

Exclusion Criteria: Patients with

- known case of epilepsy
 - Electrolyte imbalance
 - Sepsis
 - Patients having old stroke presenting with fresh stroke
 - Or any other reversible precipitating factors
- And those refusing to give informed consent for study were excluded from the study. All the patients were explained about the study and informed consent was obtained.
- Detailed clinical history and examination was done in every patient.
 - Routine investigations were done.
 - Imaging in the form of plain CT brain and/or MRI brain was performed in every patient to find out the type of lesion.

- EEG was also done in all cases to localize epileptiform foci.
- Relevant investigations were also done for determination of etiology of stroke.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams.

Age (years)	Frequency	Percentage
< 50	3	2.9
50-59	5	4.8
60-69	26	25.0
70-79	25	24.0
80-89	29	27.9
≥ 90	16	15.4
Total	104	100
Mean±SD (Range)=74.7±13.23 (28-95)		

Out of a total of 104 patients, majority i.e. 29 (27.9%) belonged to 80-89 years age group, followed by 26 (25%) patients who were aged 60-69 years, 25 (24%) patients who were 70-70 years of age. Youngest patient in our study was 23 years of age while as eldest was 94 year old.

Gender	Frequency	Percentage
Male	78	75
Female	26	25
Total	104	100
Male: Female = 3:1		

Males outnumbered the females in our study. There were 78 (75%) males and 26 (25%) females with male to female ratio of 3:1.

Time of onset of seizure	Frequency	Percentage
< 2 Weeks	63	60.6
> 2 Weeks	41	39.4
Total	104	100

Time of onset of seizure was <2 weeks in 63 (60.6%) patients while as 41 (39.4%) patients experienced the onset of symptoms at >2 weeks.

Type of Seizure	Frequency	Percentage
GTCS	67	64.4
Focal	37	35.6
Total	104	100

Majority of patients i.e. 67 (64.4%) had GTCS type of seizure and 37 (35.6%) had focal seizures.

Frequency of Seizure	Frequency	Percentage
Single	38	36.5
Multiple	66	63.5
Total	104	100

Multiple seizures were experienced by 66 (63.5%) of our study patients while as 38 (36.5%) patients had single seizure.

Status Epilepticus	Frequency	Percentage
Yes	35	33.7
No	69	66.3
Total	104	100

Status epilepticus was seen in 35 (33.7%) patients only.

Type of Stroke	Frequency	Percentage
Ischemic	60	57.7
Hemorrhagic	40	38.5
Cardioembolic	4	3.8
Total	104	100

Ischemic stroke was seen in 60 (57.7%) patients followed by haemorrhagic in 40 (38.5%) patients. Cardioembolic stroke was observed in only 4 (3.8%) patients.

Table 8: Distribution of study patients as per type of stroke

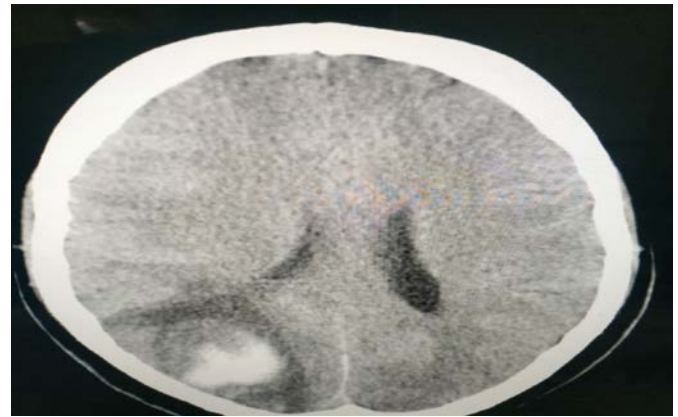
Type of Stroke	Frequency	Percentage
Arterial	101	97.1
Venous	3	2.9
Total	104	100

Arterial infarct was observed in 101 (97.1%) while as venous infarct was found in only 3 (2.9%) strokes.

Table 9: EEG findings of study patients

EEG Findings	Frequency	Percentage
Focal epileptiform activity	7	6.7
Background slowing	76	73.1
Normal EEG	21	20.2
Total	104	100

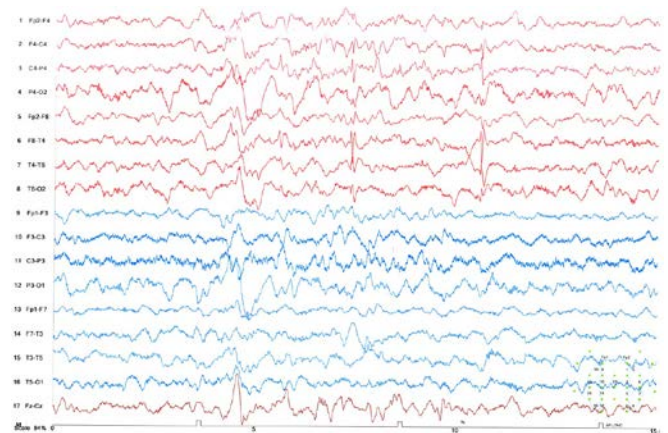
In our study, all 104 patients underwent EEG. Majority of patients i.e. 76 (73.1%) had background slowing as EEG finding. Normal EEG findings were observed in 21 (20.2%) patients while as 7 (6.7%) patients had features of focal epileptiform activity.



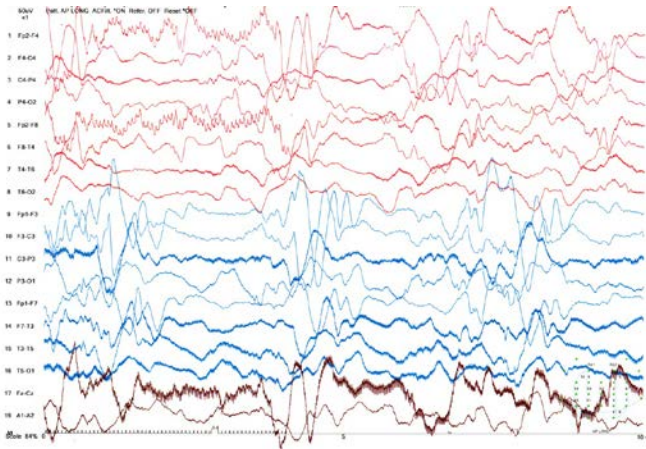
Area of bleed attenuation noted in right occipital region with surrounding edema suggestive of ?Haemorrhagic Transformation of infarct ? Venous infarct



Ill defined area of hypodensity noted in right parietal lobe suggestive of acute infarct



Abnormal EEG showing intermittent epileptiform discharges



Abnormal EEG showing background slowing with intermittent epileptiform discharge

Discussion

The relationship between seizures and stroke has been long recognized. Age-specific incidence rates of epilepsy have changed, with a decrease in younger age groups and an increase in persons above 60 years.⁹ Strokes represent the most common etiology of epilepsy in patients over the age of 60 years, with an incidence of 2-4% reported in different studies.³

Out of a total of 104 patients, majority i.e. 29 (27.9%) belonged to 80-89 years age group, followed by 26 (25%) patients who were aged 60-69 years, 25 (24%) patients who were 70-79 years of age. Youngest patient in our study was 23 years of age while as eldest was 74 year old. Similar results were obtained by **Burneo JG et al (2010)**⁴⁷ who conducted a study on 5027 consecutive patients admitted with an acute stroke with a mean age at presentation 71 years. Twenty percent patients in their study were younger than 60 years and 32% patients were older than 80 years. **Packiaseli CR et al (2017)**⁶⁰ in their study on 100 patients in which majority were 61-70 years of age which was comparable to our study.

Males outnumbered the females in our study. There were 78 (75%) males and 26 (25%) females with male to female ratio of 3:1. Similar results were obtained by

Siddiqi SA et al (2011)⁴⁹ who conducted a study on 50 subjects with post-stroke seizures in which 56% were males and 44% females. **Khealani BA et al (2008)**⁶¹ conducted a study in which males were seen more frequently as compared to females as seen in the previous international as well as regional reports.^{9,33,62} **Packiaseli CR et al (2017)**⁶⁰ in their study on 100 patients, of which 76 were male and 24 were female with a male to female ratio of (3.2:1).

Time of onset of seizure was <2 weeks in 63 (60.6%) patients while as 41 (39.4%) patients experienced the onset of symptoms at >2 weeks. **Packiaseli CR et al (2017)**⁶⁰ conducted a study on 100 patients in which early-onset seizures were present in 64 patients and late-onset in 36 patients. Of the 64 patients with early onset seizure, 50 patients (78%) had immediate onset of seizures (i.e.) within the first 24 hours of stroke. **Siddiqi SA et al (2011)**⁴⁹ conducted a study on 50 subjects in which 58% patients had early onset seizures and 42% patients had late onset seizures which is similar to the results obtained by our study.

Majority of patients i.e. 67 (64.4%) had GTCS type of seizure and 37 (35.6%) had focal seizures. Similar results were obtained by **Siddiqi SA et al (2011)**⁴⁹ who studied 50 subjects in which most commonly witnessed seizure type was generalized seizure in 37 (74%) of patients while 13 (26%) had partial seizures. **Arboix A et al (2003)**⁶³ also reported a higher frequency (50%) of generalized seizures.

Multiple seizures were experienced by 66 patients (63.5%) in our study while as 38 (36.5%) patients had single seizure. Status epilepticus was seen in 35 (33.7%) patients only. Similar results were obtained by **Siddiqi SA et al (2011)**⁴⁹ who studied 50 subjects in which 62% patients had multiple seizures while as 38%

patients had single seizures. In their study status epilepticus was seen in 1 patient (2%).

Ischemic stroke was seen in 60 (57.7%) patients followed by haemorrhagic in 40 (38.5%) patients. Cardioembolic stroke was observed in only 4 (3.8%) patients. Arterial infarct was observed in 101 (97.1%) while as venous infarct was found in only 3 (2.9%) strokes. Intracerebral hematoma was seen in 10 (20%) of subjects. Our observations are consistent with the findings of **Siddiqi SA et al (2011)**⁴⁹ who studied 50 subjects in which 40 (80%) had an ischemic stroke including 36 (72%) arterial infarct and 3 (6%) venous infarcts. A single institution study by **Rumbach L et al(2000)**¹⁹ found that 22 of 2742 patients with ischemic stroke (0.8%) had status epilepticus. In a large study of post-stroke seizures, 9% had status epilepticus.²⁰

In our study, all 104 patients underwent EEG. Majority of patients i.e. 76 (73.1%) had background slowing as EEG finding. Normal EEG findings were observed in 21 (20.2%) patients while as 7 (6.7%) patients had features of focal epileptiform activity. Our findings are comparable with the observations of **Packiaseeli CR et al (2017)**⁶⁰ who studied 100 patients and the most common EEG abnormality observed in their study was focal slowing (Type III) present in 48%. Similar correlation was observed in few studies (**Gupta SR et al., 1988**⁶⁴, **Dhanuka AK et al., 2001**³³).

Summary

The present study was conducted in the Postgraduate Department of Medicine, Government Medical College, and Srinagar.

All the adult patients over the age of 20 years, from both the genders admitted to Government Medical College diagnosed as post stroke seizures from December, 2017 to December, 2019 were included in the study.

- Out of a total of 104 patients, 27.9% belonged to 80-89 years age group, followed by 25% patients who were aged 60-69 years, 24% patients who were 70-79 years of age. Youngest patient in our study was 23 years of age while as eldest was 94 year old.
- Males outnumbered the females in our study 75% versus 25%.
- Time of onset of seizure was <2 weeks in 60.6% patients while as 39.4% patients experienced the onset of symptoms at >2 weeks.
- Majority of patients i.e. 64.4% had GTCS type of seizure and 35.6% had focal seizures.
- Multiple seizures were experienced by 63.5% of our study patients while as 36.5% patients had single seizure.
- Status epilepticus was seen in 33.7% patients only.
- Ischemic stroke was seen in 57.7% patients followed by haemorrhagic in 38.5% patients. Cardioembolic stroke was observed in only 3.8% patients.
- Arterial infarct was observed in 97.1% while as venous infarct was found in only 2.9% strokes.

In our study, all 104 patients underwent EEG. Majority of patients i.e. 73.1% had background slowing as EEG finding. Normal EEG findings were observed in 20.2% patients while as 6.7% patients had features of focal epileptiform activity

Conclusion

- GTCS are common in stroke-related seizures than partial seizures, complex partial seizures being the rarest presentation. Early-onset seizure (seizures within 2 weeks of stroke) is the most common type of stroke-related seizure.

- The pathogenesis of post stroke epilepsy is still not fully understood, but ischemic stroke is undoubtedly one of the most common reasons for epilepsy in adults. For effective prevention of post-stroke seizures and epilepsy, risk factors should be reliable and easily measured or detected in patients. Different risk factors as well as interactions between them are probably related to the development of post stroke epilepsy in a particular patient.
- Much additional work is needed to better understand the social impact of post-stroke seizures, their prevention, and effective management. Areas of the future research regarding seizures in stroke include assessing the delayed patient outcomes and developing newer antiepileptic drugs with more neuroprotective effects.

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