

Clinical and radiological profile of post-Stroke seizures

Sumit Kamble^{1,*}, Trilochan Srivastava², Vijay Sardana³, Dilip Maheshwari⁴, Bharat Bhushan⁵, Piyush Ojha⁶

^{1,6}Senior Resident, ²Professor, ³Senior Professor & Head, ^{4,5}Associate Professor, Dept. of Neurology, Govt. Medical College, Kota, Rajasthan

***Corresponding Author:**

Email: drsumitkamble@gmail.com

Abstract

Aims: To know the incidence of early versus late post stroke seizures, and its type and time of occurrence after the stroke as well as its relation with different type of stroke and location of the involvement and correlation with different risk factors along with to know occurrence early versus late post stroke seizures in young versus old stroke patients.

Study Design: Observational study.

Methodology: All the patients with the diagnosis of post-stroke seizures were included. Those with known epilepsy, sepsis, electrolyte imbalance, patient having old stroke presenting with fresh stroke and any other reversible precipitating factors were excluded. Data collected regarding the age, co-morbid conditions, details of seizures and radiological findings including type and location of stroke.

Results: Total of 100 subjects with post-stroke seizures were included. Fifty eight percent were males while 42% were females. Mean age of the study population was 57.6 ± 15 years. Eighteen patients had young stroke (<45 years) whereas rest 82 patients had age > 45 years. Early post-stroke seizures were seen in 54% of patients. Rest of the patients i.e. 46%, had late-seizures. GTCS were the most common type of seizures seen in 72% patients, followed by partial motor with secondary generalization and partial motor seen in 20% and 8% of the patients respectively. Sixty two percent of the patients had multiple episodes of seizures i.e. two or more than two episode while 38% had only single episode of seizure. Only 2% had status epilepticus. Eighty percent of the patient had Ischemic stroke while hemorrhagic stroke was seen in 20% of the patients. Sixty two percent of the patient had cortical location of stroke while 38% had subcortical location. Comparison between early and late onset seizures revealed significant association between ischemic heart disease (IHD) and hypertension with late onset seizures ($p < 0.05$). There was no significant difference in occurrence of early compared to late onset seizures in young and old patients.

Conclusion: Post-stroke seizures were more frequent in males, older age with history of hypertension, and with cortical ischemic strokes. Early seizures, multiple episodes and generalized seizure type were more common. History of ischemic heart disease and hypertension showed a strong relationship with the occurrence of late onset seizures. Long term prospective studies are required to know whether control of hypertension and IHD may lead to decrease incidence of post stroke seizures.

Keyword: Seizures, Stroke, Early versus Late Post stroke seizures.

Introduction

Stroke is one of the most common cause of morbidity and mortality across the globe and is responsible for five to six million reported deaths annually. The relationship between seizures and stroke was first recognized more than a century ago by John Hughling Jackson.⁽¹⁾ The rate of post stroke seizures ranges from 2-4%.⁽²⁾ Stroke is one of the leading cause of symptomatic epilepsy in adults.

Like stroke, post-stroke seizures (PSS) are also more prevalent in older patients and can occur after ischemic, hemorrhagic or any type of stroke. It may present in either early i.e. within 2 weeks or late i.e. after 2 weeks of stroke. Number of risk factors for post stroke seizures have been recognized in the past like male gender, age > 65 years, cortical location of lesion, larger lesion and anterior circulation infarction.^(3,4) Other reported risk factors are hemorrhagic infarcts, cerebral venous infarcts and stroke recurrence. Most studies done in past show preponderance of early over late post stroke seizures and majority presenting with focal onset seizures.⁽⁵⁾ The early seizure is associated with a high risk of status epilepticus and an increased incidence of death.⁽⁶⁾ The highest rate of late seizure is in the first year

after stroke and is related to high likelihood of developing poststroke epilepsy.⁽⁵⁾ The rate of early post stroke seizures in different studies is about 1.4-11.4 percent^(7,8) Rate of occurrence of late post stroke seizure in the patients having early post stroke seizure is approximately 32 percent and it is 10 percent in the patients without early post stroke seizures.⁽⁹⁾ Post-stroke seizures are associated with significant functional disability and mortality. Studies regarding association of risk factors for stroke with occurrence of early and late post stroke seizures are lacking. There are also only few studies done in India, moreover stroke subtypes are different in India as compared to rest of world- Cortical venous sinus thrombosis, cardioembolic stroke and young stroke are higher, so incidence of PSS may also be different.

The present study is planned aiming to know the incidence of early versus late post stroke seizures, and its type and time of occurrence after the stroke as well as its relation with different type of stroke and location of the involvement and correlation with different risk factors along with to know occurrence early versus late post stroke seizures in young versus old stroke patients in the patients admitted to Govt. Medical College, Kota.

Subjects and Methods

100 patients admitted to the Department of Neurology at a tertiary care hospital with post stroke seizures between 2015 - 2016 were enrolled in the study. Patients with known case of epilepsy, electrolyte imbalance, sepsis, patient 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 and informed consent was taken. Ethical clearance was taken from Ethical committee of the Institute. Early seizures were defined as seizures occurring within 2 weeks of stroke while late seizures were seizures which occurred 2 weeks after the stroke.

Detail clinical history and examination was done in every patient. Routine hematological investigations were done in every patient. Imaging in form of plain CT brain and/or MRI brain was performed in every patient. MRI was performed on 1.5 Tesla GE machine. EEG was also done all cases to localize epileptiform foci. Relevant investigations were also done for determination of etiology of stroke.

All the data was collected regarding onset, type and frequency of the seizure; gender and co-morbidities, radiological findings regarding type, location and nature of stroke.

All the information gathered from history, examination and neuroimaging either computed tomography (CT scan) or magnetic resonance imaging (MRI), was entered in a predefined proforma designed for the study.

Statistical Analysis

Data was analyzed using Statistical Package for the Social Sciences- SPSS 19 statistical software. Pearson chi square test was used to find relationship between the time of onset of post-stroke seizures and other variables. Significance level of 95% with $p < 0.05$ was considered statistically significant.

Results

Total of 100 subjects with post-stroke seizures were included. Fifty eight percent were males while 42% were females. The mean age of the study population was 57.6 ± 15 years. Eighteen patients had young stroke (<45 years) whereas rest 82 patients had age > 45 years. Early post-stroke seizure were seen in 54% of patients. Rest of the patients i.e. 46%, had late post stroke seizures. Generalized seizures were most common type of seizures seen in 72% patients, followed by partial motor with secondary generalization in 20% and partial motor in 8% of the patients. Sixty two percent of the patients had multiple episodes of seizures i.e. two or more than

two episode while 38% had only one episode of seizure. Only 2% of patients had status epilepticus. Eighty percent of patient had Ischemic stroke while hemorrhagic stroke was seen in 20% of the patients. Sixty two percent of the patient had cortical location of stroke while 38% had subcortical location. (Table 1). Twenty six patients had a history of Ischemic heart disease while 22 had a history of Diabetes and 62 had history of hypertension. Dyslipidemia was found in 24 patients.

Table 1 Characteristics of post-stroke seizures (n=100)

Clinical characteristics	Frequency (%)
Onset	
Early (<2 weeks)	54%
Late (>2 weeks)	46%
Type	
Generalized	72%
Partial with secondary generalisation	20%
partial	8%
Frequency	
Single	38%
Multiple	62%
Status epilepticus	
Yes	2%
No	98%
Radiological characteristics	Frequency (%)
Type of stroke	
1. Ischemic	80%
a) Arterial	74%
b) Venous	6%
2. ICH	20%
Location	
Cortical	62%
Subcortical	38%

More patients had hypertension (73.9% vs. 51.8%) and Ischemic heart disease (39.1% vs. 14.8%) in the late post stroke seizure as compared to early seizure group, which was statistically significant with p value 0.0057 and 0.023 respectively. Other comorbidities like diabetes mellitus and dyslipidemia were not statistically differed in early and late post stroke seizures groups. Age and sex had no influence on occurrence of early and late post stroke seizure group. Ischemic stroke was seen in 42 patients in early seizure group as compared to 38 patients in the late post stroke seizure group, which was statistically insignificant likewise location of lesion had no influence on occurrence of early and late post stroke seizures. (Table 2).

Table 2: Characteristics of early and late onset seizures (n=100)

Variable	Early seizures (N=54)	Late seizures (N=46)	P-Value
Gender			
Female	24(44.4%)	18(39.1%)	0.59
Male	30(55.5%)	28(60.80)	
Age			
Young (<45 years)	10(18.5%)	8(17.3%)	0.88
Old (>45 years)	44(81.4%)	38(82.6%)	
Comorbidities			
Ischemic heart disease			
Yes	8(14.8%)	18(39.1%)	0.0057
No	46(85.1%)	28(60.8%)	
Diabetes mellitus			
Yes	10(18.5%)	12(26.1%)	0.36
No	44(81.40)	34(73.9%)	
Hypertension			
Yes	28(51.8%)	34(73.9%)	0.023
No	26(48.1%)	12(26.1%)	
Dyslipidaemia			
Yes	12(22.2%)	12(26.1%)	0.20
No	42(77.7%)	34(73.9%)	
Radiological characters			
Location			
Cortical	32(59.2%)	30(65.2%)	0.37
Subcortical	22(40.7%)	16(34.7%)	
Type			
Infarct	42(77.7%)	38(82.6%)	0.54
ICH	12(22.2%)	8(17.3%)	

Discussion

Post stroke seizures were first reported in the 19th century. Hughlings Jackson in 1864 reported seizures in patient with middle cerebral artery stroke on paralysed side,⁽¹⁾ and William Gowers in 1885 first introduced the term “post-hemiplegic epilepsy”.⁽¹⁰⁾ Strokes is the most common cause of epilepsy in patients over the age of 60 years.

The incidence of post-stroke seizures varies in different studies between 4.4 to 13.8%.^(11,12,13) However slightly higher frequency i.e. 13% is reported from India by Dhanuka et al.⁽¹⁴⁾

Early post stroke seizures has been defined in various studies as seizure occurring between first 24 h to the first 4 week post-stroke. Usually early post stroke seizures occur at the onset of stroke in 1.8–15% of patients and constitute the majority of post-stroke seizures.^(11,12) The reported incidence of late post stroke seizure is approximately 2.5–15%,^(11,12,15) Recurrent seizures or post stroke epilepsy can occur in 4–9% of patients.^(16,17) Cerebrovascular disease is the most common cause of seizures in the older population: it is the cause of spontaneous seizures in approximately 36.6% of patients.⁽¹⁸⁾

Most of the post stroke seizures are focal onset and are of the simple partial Type,^(19,20) followed by primary generalized seizures. Complex partial seizures are less

common, with highest reported incidence of 24% of all post-stroke seizures.⁽²⁰⁾

The mean age was 57 years in our study which is comparable with the previous studies which reported higher incidence of PSS in middle aged or elderly patients.⁽⁵⁾ Post stroke epilepsy is rarely seen in young cryptogenic ischemic stroke survivors.⁽²¹⁾ However study in India by Dhanuka *et al* have found a younger age at first seizure after stroke⁽¹⁴⁾ (mean 45.41 years). but they had wide spectrum of patients (age range of 5 months to 76 years). In this series, males were seen more frequently as compared to females (58% vs 42%) as seen in the previous international as well as regional reports.^(14,21) However, study done by Bhojo et al. had similar frequency of post stroke seizures in males and females.⁽²²⁾

Study showed more frequency of early post stroke seizures compared to late post stroke seizures. (54 % vs 46 %), this consistent with study from India by Dhanuka⁽¹⁴⁾ et al. (77% vs 23%) and international studies Black et al.⁽²³⁾ However some studies showed more chances of late seizures as compared to early seizures Sung et al.⁽²⁰⁾

In this study most frequent type of seizure was generalized as compared to partial or secondary generalized seizures as expected in symptomatic epilepsy like PSS. This is distinct to previous data showing a preponderance of partial seizures in PSS,^(19,20)

this may be related to low education status of study population who are unable to report partial or secondary generalized seizures and misinterpret them to be generalized.

In this study 62% had multiple seizures. This is in accordance with study from India by Dhanuka *et al.* in which 60 % had multiple seizures.⁽¹⁴⁾ However some studies showed lesser rates of multiple seizures like in a prospective multicenter international study Seizures After Stroke Study Group [SASS], in which 28% of patients had multiple seizures.

In this study 2% had history of status epilepticus (SE), and all occurred in patients having early post stroke seizures. Frequency of SE is different in different studies. It was reported 14% by Milandre *et al* in patients with initial post stroke seizures⁽¹⁵⁾ whereas it was reported 10% by Lo *et al.*⁽²⁴⁾ The rate of status epilepticus was slightly lower in our study as compared to other studies but similar to other studies had more chances of SE with early post stroke seizures.

In this study, majority of patients (80%) had ischemic stroke in sharp contrast to the international data which reported an increased incidence of PSS following intracerebral hemorrhage.^(25,26) This may be due higher incidence of ischemic stroke compared to hemorrhagic stroke and observational nature of study. Long term follow up Prospective studies are needed to know exact incidence following ischemic and hemorrhagic stroke.

In this study both early and late seizures were more common with cortical lesions as compared to subcortical lesions (62% vs 38%) This is supported by previous studies in which both early and late seizures were seen more frequently seen in cortical ischemic strokes,⁽²⁷⁻²⁹⁾ while conflicting results were seen in another study by Arboix *et al.*⁽³⁰⁾

On comparing the prevalence of different risk factors and comorbidities between early and late post stroke seizures it was found that the Ischemic heart disease (IHD) and hypertension (HTN) were associated with late post stroke seizures which was statistically significant or in other words those patients who are having HTN or IHD have more chances of late post stroke seizures as compared to early post stroke seizures. In study of 50 patients by Shaista *et al* also had similar findings.⁽³¹⁾ No large prospective studies are available to know the difference in risk factors for early and late post stroke seizures. Even in the absence of clinically detected stroke, hypertension with left ventricular hypertrophy may increase the risk of unprovoked seizures.⁽³²⁾ In our study the increase risk of late post stroke seizures in patient with hypertension may be because of HTN acting as independent risk factor for seizures. However long term prospective studies are required to know the exact association of HTN and IHD with post stroke seizures and whether good control of HTN and IHD will lead to decreased incidence of post stroke seizures.

This study has a number of limitations including observational nature of the study and relatively small number of patients with post-stroke seizures. Therefore, large prospective studies are needed to know the exact association between various comorbidities and post stroke seizures and effects of better treatment of comorbidities on incidence of post stroke seizures and resultant mortality and morbidity.

Conclusion

In this study post-stroke seizures were more common in males as compared to females, older age, cortical ischemic strokes and with history of hypertension. Early post stroke seizures, primary generalized seizures and multiple episodes were more common. Patients with history of ischemic heart disease, and hypertension had strong association with the occurrence of late onset Post stroke seizures. There was no significant difference in occurrence of early compared to late onset Post stroke seizures in young and old patients. Long term prospective studies are required to know whether control of hypertension and IHD may lead to decrease incidence of post stroke seizures.

References

1. Scientific and empirical investigation of epilepsies Taylor J, ed. Selected Writings of John Hughlings Jackson. London: Hodder and Stoughton; 1931:233.
2. Epidemiology of post-stroke epilepsy according to stroke subtypes. Benbir G *et. el.* *Acta Neurol Scand* 2006;114:8-12. *Epilepsy Curr* 2007;7:42-4.
3. Cheung CM *et.al* Epileptic seizure after stroke in Chinese patients. *J Neurol* 2003;250:839-43.
4. Bladin CF, Alexandrov AV, *et al.* Seizures after stroke: a prospective multicenter study *Arch Neurol* 2000;57:1617-22.
5. Lamy C, Domigo Vet *al.* Early and late seizures after cryptogenic ischemic stroke in young adults. *Neurology* 2003;60:400-4. Comment in: p. 365-6.
6. Optimizing therapy of seizures in stroke patients. Ryvlin P, Montavont A *Neurology* 2006;67:S3-9.
7. Eoilepsy after strpke. Mervi K, Olli W. *Epilepsia* 1992;33(3):495-498.
8. Seizures at the onset of subarachnoid haemorrhage. Pinto NA, Canhao P, Ferro JM. *J Neurol* 1996;243(2):161-4.
9. Kilpatrick CJ *et al.* Early seizures after acute stroke. *Arch Neurol* 1992;49(5):509-11.
10. Epilepsy and Other Chronic Convulsive Disorders. Gowers W. 1885. Reprinted. New York: Dover;1964:106.
11. Early seizures after acute stroke: a study of 1,640 cases. Giroud M *et al.* *Epilepsia* 1994;35:959-964.
12. R. Risk factors for developing seizures after a stroke. Lancman ME, Golimstok A, Norscini J, Granillo *Epilepsia* 1993;34:141-143.
13. Bladin CF *et al.* Seizures after stroke: a prospective multicenter study. *Arch Neurol* 2000;57:1617-1622.273-276.
14. Seizures after stroke: a prospective clinical study. Dhanuka AK, *at. el* *Neurol India* 2001;49:33-6.
15. Epileptic crisis during and after cerebrovascular diseases. A clinical analysis of 78 cases. Milandre L, *at. el.* *RevNeurol* 1992;148:767-772.
16. Epilepsy after stroke. Olsen TS, Hogenhaven H, Thage O. *Neurology* 1987;37:1209-1211.

17. Risk of recurrent stroke, myocardial infarction and epilepsy during long-term follow-up after stroke. Viitanen M et al. *Eur Neurol* 1988;28:227–231.
18. A survey of epileptic disorders in southwest France: seizures in elderly patients. Loiseau J et al. *Ann Neurol* 1990;27:232–237.
19. Gupta SR, et al. Post-infarction seizures. A clinical study. *Stroke* 1988;19:1477–1481.
20. Epileptic seizures in thrombotic stroke. Sung CY, Chu NS. *J Neurol* 1990;237:166–170.
21. The epidemiology of epilepsy revisited. Sander JW. *Curr Opin Neurol* 2003;16:165–70.
22. Post-stroke seizures: descriptive study from a tertiary care centre in Pakistan. Khealani BA et al. *J Pak Med Assoc* 2008;58:365–8.
23. Post-stroke seizures. Black SE, Norris JW. *Stroke* 1983;14:134.
24. Lo YK, et al. Frequency and characteristics of early seizures in Chinese acute stroke. *Acta Neurol Scand* 1994;90:83–85.
25. Burn J et al. Epileptic seizures after a first stroke: the Oxfordshire Community Stroke Project. *BMJ* 1997;315:1582–7.
26. Arboix A et al. Predictive factors of early seizures after acute cerebrovascular disease. *Stroke* 1997;28:1590–4.
27. Stroke-related seizures and epilepsy. De Reuck. *Neurol Neurochir Pol* 2007;41:144–9.
28. So EL et al. Population-based study of seizure disorders after cerebral infarction. *Neurology* 1996;46:350–55.
29. Hornig CR et al. Epileptic seizures following ischemic cerebral infarction. *Eur Arch Psychiatry Neurol Sci* 1990;239:379–83.
30. Arboix A, et al. Relevance of early seizures for in-hospital mortality in acute cerebrovascular disease. *Neurology* 1996;47:1429–35.
31. Clinical Spectrum of Post-Stroke Seizures Shaista A. Siddiqi, Mubashira Hashmi, Farrukh S. Khan and Khurram A. *Journal of the College of Physicians and Surgeons Pakistan* 2011, Vol. 21(4):214–218.
32. Severe, uncontrolled hypertension and adult-onset seizures Hesdorffer DC, Hauser WA, Annegers JF, Rocca WA. *Epilepsia*. 1996 Aug;37(8):736–41.