

Clinical Spectrum of Post-Stroke Seizures

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ABSTRACT

Objective: To determine the characteristics of post-stroke seizures and compare these in early vs. late post-stroke seizures.

Study Design: Observational study.

Place and Duration of Study: Department of Neurology, Liaquat National Hospital, Karachi, from March to September 2007.

Methodology: All admitted patients aged over 25 years, with diagnosis of post-stroke seizures were included. Those with known epilepsy, sepsis and electrolyte imbalance were excluded. Age, co-morbid condition, details of seizures and radiological findings regarding type and location of stroke were collected and entered in a pre-formed proforma. Results were described as frequency and mean. Association of variables was determined through chi-square test with significance at $p < 0.05$.

Results: Out of the 50 patients, there were 28 (56%) males and 22 (44%) females with the mean age of 56.86 ± 15.26 years. Thirty-one (62%) patients had history of hypertension. Early seizures i.e. within 2 weeks were seen in 29 (58%) patients. Generalized seizures were seen more frequently i.e. in 37 (74%) patients. Thirty-one (62%) subjects experienced more than 2 seizures. Forty (80%) had an ischemic stroke including 36 (72%) arterial infarct and 3 (6%) venous infarcts. Intracerebral hematoma was seen in 10 (20%) of subjects. Comparison between early and late onset seizures revealed significant association between ischemic heart disease (IHD), old stroke, hypertension and late onset seizures ($p < 0.05$).

Conclusion: Post-stroke seizures were more frequent in males, with history of hypertension, and with cortical ischemic strokes. Early seizures, multiple episodes and generalized seizure type were more common. Venous infarcts were chiefly associated with seizures at presentation. History of old stroke, ischemic heart disease, hypertension and hypercholesterolemia showed a strong relationship with the occurrence of late onset seizures.

Key words: Ischemic stroke. Haemorrhagic stroke. Post-stroke seizures. Cortical infarct. Venous infarct.

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. The relationship between seizures and stroke was recognized more than a century ago by John Hughling Jackson.² 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 (PSS) 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 PSS.^{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

Since there is sparse data on post-stroke seizures from Pakistan apart from a retrospective study,¹⁰ this study was conducted to determine the characteristics of post-stroke seizures and compare these in early vs. late post-stroke seizures.

METHODOLOGY

This study was conducted at the Department of Neurology, Liaquat National Hospital, Karachi between March and September 2007. It was an observational study and patients were prospectively recruited via non-

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probability convenience sampling. It comprised of all adult patients over the age of 25 years, from both the genders, who were admitted in this department and were diagnosed to have post-stroke seizures. Patients who were known epileptics or had metabolic abnormalities like sepsis and electrolyte imbalance were excluded.

Early seizures were defined as seizures occurring within 2 weeks of stroke while late seizures were seizures which occurred 2 weeks after the stroke.⁹ Cortical stroke were defined as lesions that were either cortical or cortico-subcortical (partial or total involvement of the supratentorial arterial territories). Subcortical stroke were defined as lesions which were exclusively subcortical.

Data was collected regarding type, onset and frequency of the seizure, radiological findings regarding type, location and nature of stroke; gender and co-morbidities. Information gathered from history, examination and radiological findings, as on computed tomography (CT scan) or magnetic resonance imaging (MRI), was entered in a proforma especially designed for the study.

Statistical data was analyzed on Statistical Software package SPSS version 10. Descriptive statistics were applied to calculate the frequencies and percentages of categorical variables such as gender, nature of stroke, type of seizures and radiological findings. Mean \pm standard deviation was calculated for continuous variables like age.

Pearson's chi-square test and Fisher exact tests were applied accordingly to find relationship between the time of onset of post-stroke seizures and other variables. P-value of < 0.05 was considered statistically significant.

RESULTS

A total of 50 subjects with post-stroke seizures were included. There were 28 (56%) males and 22 (44%) females. Mean age was 56.8 ± 15.26 years. Twenty-three (46 %) patients had a history of previous stroke while 31 (62%) had a history of hypertension. History of Diabetes and ischemic heart disease (IHD) was present in 12 (24%) and 14 (28%) of the total subjects respectively (Table II). Hypercholesterolemia was found in 11 (22%) of patients. Thirty-seven (74%) had hemiparesis at the time of examination while altered mental status and dysphasia was seen in 15(30%) and 22 (44%) patients respectively.

Early post-stroke seizure were seen in 29 (58%) of patients. Rest of the subjects i.e. 21 (42%), experienced late-seizures. Most commonly witnessed seizure type was generalized seizure in 37 (74%) of patients while 13 (26%) had partial seizures. Thirty-one (62%) patients experienced more than two seizures. Status epilepticus was seen in only one subject (2%) who was a young male with a large intracerebral hematoma (Table I).

A large proportion of patients, 40 (80%) had an ischemic infarction as evidenced by CT scan or MRI brain. Of ischemic strokes, 37 (74%) had an arterial infarct while venous infarct was found in only 3 (6%) of the subjects who were all young females. Intracerebral hematoma was seen in 10 (20%) of subjects (Table I).

Table I: Characteristics of post-stroke seizures (n=50).

Clinical characteristics	n (%)
Onset	
Early (< 2 weeks)	29 (58)
Late (> 2weeks)	21 (42)
Type	
Generalized	37 (74)
Partial	13 (26)
Frequency	
Single	19 (38)
Multiple	31 (62)
Status epilepticus	
Yes	1 (2)
No	49 (98)
Radiological characteristics	
Type of stroke	
Infarct	40 (80)
a. Arterial	37 (74)
b. Venous	3 (6)
ICH*	10 (20)
Location	
Cortical	29 (58)
Sub cortical	21 (42)

Almost equal proportion of either gender i.e. 14 males and 15 females, was seen in the early seizure group. However, males were more frequently seen, 14 (66.66%) subjects, in the late seizure group (Table II). In the early seizure group 6 patients presented with altered mental status, 22 with hemiparesis while 12 patients had dysphasia on examination. History of past stroke was significantly higher in late onset seizures i.e. 17 (80.9%) patients as compared to only 6 (20.6%) patients in early seizure group. Also more patients had hypertension (80.9% vs. 48.2%) and hypercholesterolemia (36% vs. 10%) in the late-seizure as compared to early seizure group. This trend was also seen in case of diabetes (28.5% vs. 20.6%) as well as ischemic heart disease (42.8% vs. 17.2%). Statistically significant p-values were achieved for ischemic heart disease (0.04), hypertension (0.01) and old stroke (0.001). P-value for type of stroke was 0.88.

Generalized seizures were seen in 22 (75.8%) patients in early seizure group as compared to 7 (24.1%) subjects with partial seizures. In the late seizure group, 15 (71.4%) patients had generalized seizures versus 6 (28.5%) patients who had partial seizures. Most patients experienced more than one seizure; 17 (58.6%) in the early as compared to 14 (66.6%) in late seizure group. The only patient who had status epilepticus had early seizures within 24 hours of stroke onset.

Ischemic stroke was seen in 23 patients in early seizure group as compared to 17 subjects in the late seizure group. Of the ischemic strokes, 3 patients had venous infarct –all with early seizures within 24 hours. Cortical infarct was seen more in early seizure group as compared to late seizure group (18 vs. 11 patients). Distribution of subcortical infarcts showed an opposite trend in the early and late seizure group (Table II).

Table II: Characteristics of early and late onset seizures.

Variable	Early seizure (n=29)	Late seizure (n=21)	p-value
Gender			
Female	15 (51.72%)	7 (33.33%)	0.19
Male	14 (48.27%)	14 (66.66%)	
Comorbids			
Old stroke			
Yes	6 (20.68%)	17 (80.95%)	< 0.00 [^]
No	23 (79.31%)	4 (19.04%)	
IHD**			
Yes	5 (17.24%)	9 (42.85%)	0.04
No	24 (82.75%)	12 (57.14%)	
Diabetes mellitus			
Yes	6 (20.68%)	6 (28.57%)	0.05
No	23 (79.31%)	15 (71.42%)	
Hypertension			
Yes	14 (48.27%)	17 (80.95%)	0.01 [^]
No	15 (51.72%)	4 (19.04%)	
Radiological findings characteristics			
Location			
Cortical	18 (62.06%)	11 (52.38%)	0.4
Subcortical	11 (37.93%)	10 (47.61%)	
Type			
Infarct	23 (79.31%)	17 (80.95%)	0.88 [^]
ICH*	6 (20.69%)	4 (19.04%)	

* ICH = Intracerebral hematoma; ** IHD = Ischemic heart disease.
[^] p-value calculated by Fisher's exact test.

DISCUSSION

The relationship between seizures and stroke has been long recognized.² 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 Bhojo *et al.* have estimated the frequency of post-stroke seizures, in a setting similar to the present to be 8% (117 of the 1548 subjects admitted with stroke).¹⁰ Of these, 24 (21%) continued to have seizures at one year follow-up. A slightly higher frequency i.e. 13% is reported from India.¹³ Conversely, a lower frequency is reported from China i.e. 3.4%.⁵

Systematic reviews suggest that seizures related to intracerebral haemorrhages occur in 10.6%, while those related to ischemic stroke appear in 8.6%. Early seizures crop up significantly more often in patients with haemorrhagic strokes and have a poor prognosis with a

high in-hospital mortality rate; however, the recurrence rate is low. Late seizures occur mainly between 6 months and 2 years after stroke with a high recurrence rate. Patients with a partial anterior circulation syndrome, a large cortical infarct with irregular borders, located in the parieto-temporal regions, are mainly at risk.¹¹ Late onset of the first seizure is an independent risk factor for epilepsy after ischemic stroke but not after haemorrhagic stroke.⁶ As many as 20% of seizures, occurring in patients with a previous cerebral infarct, may prove later as a clinical expression of a new stroke.¹¹ Seizure at the onset of a first-ever stroke was found to be an independent prognostic factor for in-hospital mortality.¹² Arboix *et al.* proposed that patients with the highest risk of developing epileptic seizures are aged persons with a large haemorrhagic infarction of a parietal lobe, who may be the candidates to be treated prophylactically with anti-epileptic medications for few days.¹²

The mean age of 56 years in this series is consistent with the previously reported increased incidence of PSS in middle aged or elderly patients.⁷ Epilepsy is rarely a major problem in young cryptogenic ischemic stroke survivors.⁹ Dhanuka *et al.* have found a younger age at first seizure after stroke (mean 45.41 years) but they have enrolled a wide spectrum of patients (age range of 5 months to 76 years).⁹ In this series, males were seen more frequently as compared to females as seen in the previous international as well as regional reports.^{9,13,14} However, Bhojo *et al.* have observed the same frequency of post-stroke seizures regarding gender in their series.¹⁰

Forty-six percent patients of this series had an old stroke as noted in a previous series by Henny *et al.*^{15,16} Hypertension was the single most common co-morbid, encountered in all subjects with PSS. This is supported by previous data.

In this study, majority of patients (80%) had ischemic infarct strikingly similar finding as compared to local data¹⁰ but in sharp contrast to the international data which reported an increased incidence of PSS following intracerebral haemorrhage.^{17,18}

Interestingly most frequent seizure type was generalized. Again similar to local data,¹⁰ 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

There was only a single case of status epilepticus in this series, a young male patient with acute large cortical hematoma. Also early seizures were encountered more frequently as compared to the other hospital-based series which reported a lower incidence of early PSS.^{10,20} Also, multiple seizures were seen more with ischemic strokes which may be a reflection of a preponderance of ischemic stroke in this cohort.

Both early and late seizures were seen more frequently in cortical ischemic strokes as supported by previous studies,^{10,21,22} while conflicting results were seen in another study by Arboix *et al.*¹² This is also in contrast to other reports, mostly representing the Western population, which have shown haemorrhagic infarct more in association with late seizures.^{17,23,24}

Out of the 10 patients with intracerebral hematoma (ICH), 6 (60%) had an early seizure. This is a higher rate when compared to respective data. A retrospective study dealing with PSS in spontaneous ICH, found early seizures in 42.9% patients. Also, focal seizures were seen in 75.7%, SE in 21.4% and recurrence in 28.6% of the patients. Lobar hematoma was present in 78.6%; of which 57% involved the frontal lobe.²⁴ In an Italian study including 761 patients with ICH and 57 patients having had one or more seizures, early seizures were associated with lobar location and rebleeding. In addition, alcohol abuse was found to be a risk for status epilepticus.²⁵ However, the present sample size is inadequate to draw upon any compact results.

Amongst the ischemic stroke, only 3 (6%) subjects had a venous cause, and all of them had seizures within 24 hours of presentation. This relationship of seizures and venous infarction is well established.³ However, the site of stroke had no significant association with the time of onset of seizure.

Also seen, was the frequent and significant existence of other comorbidities like old stroke, ischemic heart disease, hypertension and hypercholesterolemia especially in cases of late onset seizures.

This study has a number of limitations including a relatively small number of patients with post-stroke seizures, which limits the ability to draw any causative associations among variables. Also this study lacks the EEG data, which might have helped us in identifying more seizures including non-convulsive seizures or status epilepticus; as well as the information regarding the antiepileptic treatment given to these subjects and their outcome. Therefore, larger-sized prospective studies are obligatory to improve the understanding of the post-stroke seizures and their impact on the person and society, translating into a better and evidence-based health care provision.

CONCLUSION

Post-stroke seizures were more frequent in males, with history of hypertension, and with cortical ischemic strokes. Early seizures, multiple episodes and generalized seizure type were more common. Venous infarcts were chiefly associated with seizures at presentation. History of old stroke, ischemic heart disease, hypertension and hypercholesterolemia showed a strong relationship with the occurrence of late onset seizures.

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