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A study of predictors of onset of seizure and predominant seizure type in post stroke patients

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Abstract
Introduction: Previous studies have reported that post stroke seizure (PSS) accounts for 4% to 10% cases. Many of these data were based on retrospective studies often without CT confirmation of lesion. Often included patients were those of arterio-venous malformations, brainstem strokes, subarachnoid hemorrhages or patient with a previous history of seizure or epilepsy. In present study we evaluated the predictors of onset of seizure and predominant seizure type in patients of PSS.
Materials and Methods: Fifty patients of PSS were studied in Hamidia Hospital from December 2017 to April 2018. CT scan and EEG were performed in all the patients. CT finding were categorized as Infarction and hemorrhage. Infarcts were sub classified as cortial and subcortical (Small as <5cm and Large >5cm). Hemorrhage was also noted for their location and volume (Small as 0-29 ml and Large as 30 ml or more). EEG findings are categorized as Normal; Diffuse slowing, Focal Slowing and Epileptiform discharges.
Results: PSS was more common in the age group of >60 years (64%)]. Majority of the patients had hemorrhagic stroke (62%). Early onset seizure occurred in 72% and late onset occurred in 28% of patients. Focal seizures were seen in 54%, generalized seizure in 24% and 10% patients developed status epilepticus. In Early onset seizure 44% were focal, 30.6% were generalized and all 5 cases of status epilepticus were early onset. Among late onset 71.4% were focal. Cortical location (68.4%) was commonly associated with PSS. Lobar hemorrhages were the most common cause of PSS (77.4%) and among them deep hemorrhage (78%) was most common. Among the ischemic stroke patients, large lesion was majorly associated (63.2%) whereas among hemorrhagic stroke patients, large size of lesion was associated with 83.8% PSS patients. Mortality was reported only in patients with early onset seizure.
Conclusion: We conclude that PSS is more common in hemorrhagic stroke. Early onset of post stroke is most common. Corticle localization is seen in ischemic stroke. Lobar localization is associated with increased risk of PSS in hemorrhagic stroke. Size of lesions is an important risk factor for PSS. Among the subtype focal seizure is most common. Mortality was mainly seen in early onset of seizure patients and patients with status epilepticus.

Keywords: status epilepticus, lobar hemorrhages, early onset seizure, mortality

Introduction
Seizures secondary to stroke have been recognized for many years and are considered as a major cause of epilepsy in elderly. The frequency of seizures after stroke is variously estimated between4% to 10% [1].
Previous assumptions such as seizures being more frequent in cerebral hemorrhagic or cardioembolic stroke 4 are not evidence based [2]. Results of population based studies using multivariate analysis have indicated that risk factors for PSS include hemorrhagic stroke, cortical location of stroke and severity of stroke. Other studies have proposed that the risk of epilepsy is greater in patients with late onset seizure after stroke, and early onset seizures are considered as risk factor for stroke related death [3].
The relation between seizures and stroke was recognized more than century ago by John Hulging Jackson (Father of Neurology). However there have been very few prospective study to define incidence of seizures in stroke, there clinical pattern, response to therapy and outcome [4].
A smaller prospective or case control studies are less valid as a source of incidence data, still they provide very useful information about risk factors predictors and clinical characteristics. There have been very few studies that define patterns and outcomes of seizure after stroke. An effort has been made to study predictors of onset of seizures after stroke and predominant seizures type with respect to clinical features, CT scan findings, EEG correlation in patients of post stroke seizures (PSS).

Materials and Methods
Fifty patients of PSS were studied who were admitted in Hamidia Hospital or who were presented in Neurology OPD of Hamidia Hospital from December 2017 to April 2018.
All patients of stroke who were admitted in Hamidia Hospital and developed seizure, patients with the complaints of seizure who had previous history of stroke (CT scan proven) and all patients of post stroke seizure attending neurology OPD or epilepsy clinic were included. Patients with age less than 15 years, previous episode of seizure (before stroke), previous brain surgery, head trauma, brain tumor, sub arachnoid hemorrhage or AV malformation related bleed/ CVT and patients having significant metabolic abnormality (hypoglycemia, severe hyperglycemia, hyponatremia, uremia, alcohol intoxication and hepatic encephalopathy) were excluded from the present study.
Seizures were classified as generalized focal with or without

secondary generalization, presence or absence of status epilepticus and frequency and recurrence. As per timing of occurrence of seizure after stroke, seizure are classified as Early (those occurring within two weeks of stroke) and Late (those occurring after two weeks of stroke). Early onset seizures are further sub classified into Immediate or onset seizure (if seizure occurred within 24 hours of stroke), Recurrent seizures (those occurring at least two weeks after the onset of initial seizure) and two or more than 2 seizures are considered as multiple.

CT scan and EEG (except in critically 14 patients) are performed in all the patients. Other investigation performed as and when required. CT finding were categorized as Infarction and hemorrhage. Infarcts were sub classified as cortial and subcortical (Small as <5cm and Large >5cm). Hemorrhage was also noted for their location and volume (Small as 0-29 ml and Large as 30 ml or more). EEG findings are categorized as Normal; Diffuse slowing, Focal Slowing and Epileptiform discharges.

An attempt was made to avoid medication for prevention of seizure in patients admitted with stroke only and to use only single medicine if required.

All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was performed to prepare the tables. Data is expressed as number and percentage. Microsoft office and PRISM software were used to prepare the graphs.

Results

PSS was more common in the age group of >60 years [32 (64%)]. Majority of the patients had hemorrhagic stroke (62%) followed by ischemic stroke (38%).

Table 1: Seizure onset according to stroke subtype

Stoke type	Early onset [36 (72%)]		Late onset [14 (28%)]
	Within 24 hours	24 hours-2 weeks	>2 weeks
Ischemic	9 (69.2)	4 (30.8)	6 (31.6)
Hemorrhagic	18 (78.3)	5 (21.7)	8 (25.8)

Data is expressed as no of patients (percentage).

Table 2: Seizure onset according to type of stroke

Subtype of stroke	Focal seizure	Focal seizure with secondary generalization	Generalized seizure	Status epilepticus
Ischemic	13 (68.4)	1 (10.8)	3 (15.8)	1 (5.2)
Hemorrhagic	14 (48)	4 (13)	9 (29)	4 (13)
Total	27 (54)	6 (12)	12 (24)	5 (10)

Data is expressed as no of patients (percentage).

Table 3: Types of seizure according to seizure's onset

Onset	Focal seizure	Focal seizure with secondary generalization	Generalized seizure	Status epilepticus
Early (n=36)	16 (44.4)	4 (11.1)	11 (30.6)	5 (13.9)
Late (n=14)	10 (71.42)	2 (14.3)	1 (7.1)	0 (0)

Data is expressed as no of patients (percentage).

Cortical location (68.4%) was commonly associated with PSS. Lobar hemorrhages were the most common cause of PSS (77.4%) and among them deep hemorrhage (78%) was most common.

Among the ischemic stroke patients, large lesion was majorly associated with PSS (63.2%) whereas among hemorrhagic stroke patients, large size of lesion was associated 83.8% PSS patients.

Table 4: Comparing types of seizure with size of lesions

Seizure type	Ischemic		Hemorrhagic	
	Large	Small	Large	Small
Focal seizure	8 (66.7)	5 (71.4)	12 (46.15)	2 (40)
Focal seizure with secondary generalization	2 (16.6)	2 (28.6)	3 (11.5)	1 (20)
Generalized seizure	3 (28)	0(0)	7 (26.9)	2 (20)
Status epilepticus	1(8.03)	0(0)	4 (18.4)	0(0)

Data is expressed as no of patients (percentage).

Focal slowing was reported in 46.6% of patients. 40% of ischemic subgroup had focal slowing while 53.3% of hemorrhagic subgroup had focal slowing. Normal EEG findings were seen in 43.3% patients. Epiletiform discharge was seen in 4% patients only.

In present study mortality was seen only in patients with early onset seizure. Among the patients who died, 80% belonged to hemorrhagic subgroup and 20% belong to ischemic subgroup. All patients of status epilepticus died during the hospital stay.

Discussion

PSS are the most common cause of seizure in elderly in various clinical studies. We planned this study to study the predictors of onset of PSS and to study predominant seizure type in the PSS. Majority of the previous studies performed till dates have studied early PSS only; those that occurred 2 or less than 2 weeks and late as those occurring after more than 2 weeks. But majority of them are from the western countries. Studies on Indian PSS patients are limited. In present study we also considered the same criteria and conducted a study which comprised of 50 patients of PSS.

We found that early PSS was more common than late. 72%

(36/50) patients had early seizures while 28% had late seizures. Similar types of findings were reported by Louis *et al*. [5] They found that 60% of patients had early PSS and 40% patients had late PSS. They took demarcation period of one week between early and late seizures. In another study conducted by Gupta *et al*. [6] which considered a demarcation period of 2 weeks, found that late seizures were the predominant type with 67% and early seizures were seen in 33% of patients.

The findings were consistent with our finding but with a variable demarcation period between early and late PSS; Lancman *et al*. [7] considered a demarcation period of 30 days, Gourd *et al*. [8] of 15 days, Arborix *et al*. [9] of 82 days, Reith *et al*. [10] of 14 days and Burn *et al*, [11] of less than 24 hr. Therefore there may be variability in the findings. Depending on all the studies mentioned, the frequency of early PSS in the largest studies was in the range from 2% to 33% with 50% to 78% occurring within 24 hours of stroke.

In this study the seizure occurrence within 24 hours (onset seizure) was found in 75% (27/36) of patients of early seizures (69.2% in ischemic subgroup and 78.3% in hemorrhagic subgroup. From this study it was derived that PSS was more common among hemorrhagic stroke (62%) than in patients of ischemic stroke (38%). This is supported by various studies such as Richardson *et al*, [12] and Kotila *et al*. [13] They conducted a retrospective study of 200 stroke patients and found that occurrence of epilepsy was more common in ICH then in ischemic stroke. This study was also supported by large oxfordshire community project [11] which included 675 patients of stroke with follow up of 2-6.5 years. The risk of seizure was increased in survivors of ICH with respect to patients of Ischemic stroke. Similar results were seen in large prospective study conducted by Bladin *et al*. [14] Kevin *et al*. [15] also reported increased frequency of early seizure in patients of hemorrhagic stroke (10.6%) as compared to ischemic stroke (8.6%). Two studies viz. Dhanuka *et al*. [16] and Misirli H *et al*. [17] concluded that PSS were more common in ischemic stroke than hemorrhagic stroke.

In the present study independent predictors for early seizure were found to be size of lesion. In ischemic group 88.3% patients had early seizure as compared to 42.8% in patient with small lesion size. In hemorrhagic group 76% had early seizure is large hemorrhage as compared to 60% in patients with small hemorrhage. The above finding is supported by Gupta *et al*. [6] and Dhanuka *et al*. [16]

It is seen that cortical location of lesion is the major risk factor for early seizure in both ischemic as well as hemorrhagic stroke. 68.4% patients of ischemic stroke developed seizure among which early seizure was predominant, similarly 77.4% patients of hemorrhagic stroke with lobar hemorrhage developed seizure. We divided lobar hemorrhage into superficial and deep. The cortical location as a predictor of early onset seizure had been observed in various other studies. Giourd *et al*. [8] concluded the loss of consciousness and cortical location as predictor for ES. Burn *et al* [11] and Arborix *et al*. [9] also supported cortical location of seizure to be an independent risk factor for developing PSS. Previous studies like Reith *et al*. [10] and Bladin *et al*. [14] also supported the present study findings.

Data regarding seizure subtype (simple partial, complex partial, partial seizures with secondary generalization and generalized seizure) is limited due to retrospective design of majority of studies and moreover confounded by interviewer and recalls bias related to obtaining seizure descriptions from patient and observer. Up to 63% of seizure may not be recognized by patient therefore different frequencies of seizures subtypes after stroke has been found in different studies. In this study the most common types of seizure was found to be focal seizure accounting for 54% of total PSS followed by generalized seizures (24%).

In present study, 10% of patients were having status epilepticus. Most common type of seizure in early onset group was focal seizure (44.4%) while 30.6% patient had generalized seizure. Of the five patients who were presented with status epileptics all were early onset type. Most common type of seizure in late onset type was also focal seizures. This study was supported by several other studies like Baldin *et al*. [14], Burn *et al*. [11] Kilpatric and Coworkers [18], Gourd *et al*. [8], Dhanuka *et al*. [16] which concluded that generalized tonic clonic seizure were the most commonly type of seizures.

In the present study 30 patients underwent EEG. Most common finding was focal slowing (46.4%) while 43.3% patients had normal EEG finding. Only 2 patients had epileptiform discharges. Homer *et al*. [19] concluded that 88% patients had EEG abnormalities among which focal slowing was most common. Carrera *et al*. [20] studies 100 patients with stroke with continuous EEG monitoring using 10 electrode epileptic activity occurred in 17 patients and most common was repetitive focal activity.

In present study in hospital mortality was seen among 20 patients of PSS. All of these mortality occurred in patients with early PSS; 21.0% patients were having ischemic stroke while 51.6% patients had hemorrhagic stroke. All the patients of status epilepticus died during the hospital period. Gupta *et al*. [6] found higher mortality at 48 hours among patients with early seizure (30.8%) versus those without early seizure. Vespa *et al*, [21] found that seizures are independently associated with increased midline shift after intra-parenchymal hemorrhage. Rumbach *et al*. [22] found that immediate prognosis is poor in patients with status epilepticus. Further study regarding pathophysiology, epidemiology, risk factors and treatment is required a large multivariate prospective studies are required for further information regarding post stroke seizures.

Conclusion

PSS is more common in hemorrhagic stroke. Early onset of post stroke is most common. Corticle localization is seen in ischemic stroke. Lobar localization is associated with increased risk of PSS in hemorrhagic stroke. Size of lesions is an important risk factor for PSS. Among the subtype focal seizure is most common. Mortality was mainly seen in patients with early onset of seizure and patients with status epilepticus. A further large randomized clinical trial is required to strengthen the present study findings.

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