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ORIGINAL ARTICLE

Post-stroke Seizures: A Prospective Study from a tertiary care setting in Karachi

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ABSTRACT

Aim: To determine the frequency and outcome of seizures after acute ischemic stroke in a tertiary care setting in Pakistan.
Methodology: A prospective, cross-sectional study was done at Liaquat National Hospital over a year. The outcome of interest was the occurrence of seizures during the one-year follow-up and death following stroke. Data was compiled and analyzed using IBM SPSS Statistics version 26. Mean and standard deviations were calculated for the quantitative variables. Frequencies and percentages were reported for the qualitative variables. Effect modifiers were controlled through stratification to see the effect of these on outcome variables by chi-square and Fisher exact test. Odds ratios were calculated by binary logistic regression.
Results: A total of 126 patients were involved with acute ischemic stroke, 74(58.7%) of them were men. Patients' average age was 62.20±13.86 years, with 69(54.8%) of them being over 60. Seizures were observed in 14(11.1%) of patients, with most being early-onset 12(85.7%). The type of seizures observed included partial seizures in 10(71.4%) of cases and generalized seizures in 4(28.6%). Patients who have seizures are more likely to die than patients without seizures (OR=1.742, p=0.372).
Conclusion: The reported occurrence of post-stroke seizures in our study is in line with what has been described in earlier research conducted on a global scale. Notably, our study identified a higher prevalence of early-onset seizures, with partial seizures being more common than generalized seizures in our findings.
Keywords: Seizures, stroke, follow-up study

INTRODUCTION

Acute ischemic stroke is a major cause of mortality and morbidity worldwide, leading to a significant healthcare burden. While the immediate management and prevention of recurrent strokes have been extensively studied, less attention has been given to the occurrence and outcomes of seizures following acute ischemic stroke. Understanding the frequency and outcomes of seizures after acute ischemic stroke is crucial for optimizing patient care and improving prognostic evaluation.

Seizures following a stroke have been classified as either early-onset (ES) or late-onset (LS) seizures. According to the International League Against Epilepsy, early-onset seizures (ES) were defined as seizures occurring within seven days after stroke onset, and late-onset seizures (LS) were defined as seizures occurring after this period.[1] Early-onset seizures are also considered provoked seizures when associated with acute ischemic infarction, occurring due to electrolyte disturbances, induced by medications, while late-onset seizures are thought to be unprovoked seizures that originate in regions of partially damaged brain tissue where neuronal networks have altered anatomically and physiologically after the stroke[2,3].

The frequency of post-stroke seizures has been reported from 5-10% in the West[4-7]. A slightly higher frequency i.e. 13% is reported fromIndia[8]. A lower frequency is reported fromChinai.e. 3.4%[8]. Several risk factors are identified in the literature for post-stroke seizures such as cortical involvement, large lesions[9,10] infarcts due to cardiogenic embolus[11] male gender[11]and stroke disability and old age[6].

Stroke subtypes play a huge role in post-stroke complications and management and fall under two broad categories, cortical and subcortical. Corticalis usually due to an atherothrombotic or embolic occlusion in major extracranial or intracranial cerebral vessels while subcortical is due to occlusion of smaller penetrating arteries or arterioles supplying the subcortical white matter. Some strokes can also be combined and include both cortical and subcortical areas and hence are the most dangerous category leading to more serious complications than just cortical or subcortical alone[12]. Cortical involvement has been reported as the most important predictor of development of post-stroke seizures, in acute ischemic strokes[13,14].

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According to a review done in 2016, mortality was found to be greater in patients who had early seizurespost-ischemicstroke.[1] Theincidenceoffocaltobilateralconvulsiveseizureswas57.1% while focal aware and focal impaired awareness seizures occurred in 42.9% of the patients. The EEG reported focal or diffuse slowing of background activity in most patients, with a higher incidence of focal temporal abnormalities[2].

In terms of medical management of seizures, studies have shown that carbamazepine, gabapentin and lamotrigine have similar efficacy, however, lamotrigine had fewer side effects. Lamotrigine and carbamazepine were also compared and the results revealed lamotrigine to be clinically better. Additionally,both levetiracetamand carbamazepine haveshownimprovementinlate-onsetpost- stroke seizures with fewer adverse effects reported in patients with levetiracetam[15].

This study aims to conduct a comprehensive investigation of seizures after acute ischemic stroke in a tertiary care setting. The findings will contribute to the existing literature on post-stroke seizures, particularly in the context of the local population. The results will aid in developing effective strategies for the prevention, management, and prognostication of seizures in acute ischemic stroke patients. Ultimately, the goal is to improve patient outcomes and enhance the quality of stroke care in our region.

METHODOLOGY

This study aimed to investigate the development of seizures and mortality after stroke in a cross- sectional design conducted at Liaquat National Hospital and Medical College (LNH&MC) over one year. Permission was granted by Hospital Ethical Committee. The outcome of interest was the occurrence of seizures during the one-year follow-up and death following stroke. The inclusion criteria encompassed all patients admitted with acute ischemic stroke, while exclusion criteria included subarachnoid hemorrhage, intracerebral hemorrhage, cerebral venous sinus thrombosis, arteriovenous malformation, previous history of seizures or epilepsy before the stroke, and toxic-metabolic causes of seizures. Data collection involved the enrollment of acute ischemic stroke patients admitted to the neurology ward at LNH. Neuroimaging, such as CT Head or MRI Brain, was performed within 24 hours of admission to record demographic data, risk factors, stroke type and severity, as well as the size and location of the lesion.

The occurrence of post-stroke seizures was determined by studying outpatient follow-up case notes and conducting telephone

contacts for patients who were lost to follow-up in clinics. Detailed history taking, physical examination, and additional investigations, including EEG, were conducted during outpatient visits when seizures occurred. The type, onset time, recurrence, and initiation of anti epileptic drugs (AEDs) were recorded. The follow-up duration was one year. Data were compiled and analyzed using the SPSS version 25.

Quantitative variables were summarized using mean and standard deviations, while qualitative variables were presented as frequencies and percentages. Effect modifiers were controlled through stratification to assess their impact on outcome variables. The significance of associations was evaluated using the post-stratification chi-square test with a p-value of ≤0.05 considered statistically significant.

RESULTS

In the current study, a total of 126 patients were involved with acute ischemic stroke, 74(58.7%) of them were men. Patients' average age was 62.20±13.86 years, with 69 (54.8%) of them being over 60. Among our patients, we discovered 75 (59.5%) had cortical strokes, 36 (28.6%) had subcortical strokes,and15(11.9%) had both cortical and subcortical strokes. According to NIHSS standards, 32(25.4%) of patients had minor strokes, 57(45.2%) had moderate strokes, 24(19%) had moderate to severe strokes, and 13(10.3%) had severe strokes while the death rate was 50(39.7%). We discovered that 100(79.4%) of patients had hypertension, 59(46.8%) had diabetes mellitus, 13(10.3%) had dyslipidemia and14(11.1%) had seizures. Out of the14 patients with seizures, 12(85.7%) experienced early-onset seizures, while 2 (14.3%) had late-onset seizures. The type of seizures observed included partial seizures in 10(71.4%) of cases and generalized seizures in 4 (28.6%). Anti-epileptic drugs were given to 9 (7.1%) of the patients.

Table1: Descriptive statistics of the study population

	n(%)
Gender	
Male	74(58.7)
Female	52(41.3)
Age(years); mean±std.dev	62.20±13.86
Age Group	
≤45years	15(11.9)
46-60years	42(33.3)
>60years	69(54.8)
Stroke Type	
Cortical	75(59.5)
Subcortical	36(28.6)
Cortical/Subcortical	15(11.9)
Severity of stroke-NIHSS	
Minor	32(25.4)
Moderate	57(45.2)
Moderateto Severe	24(19)
Severe	13(10.3)
Types of strokes	
ACA Present	19(15.1)
MCA Present	92(73)
PCA Present	18(14.3)
Vertebrobasilar Present	100(79.4)
Co-morbidities	
Hypertension	100(79.4)
DiabetesMellitus	59(46.8)
Dyslipidemia	13(10.3)
Seizures	14(11.1)
Onset Seizure (n=14)	
Early	12(85.7)
Late	2(14.3)
Type of Seizure (n=14)	
Partial	10(71.4)
Generalized	4(28.6)
Outcome	
Alive	76(60.3)
Expired	50(39.7)

Most of them had received Levetiracetam 6(66.6%). EEGs were performed on 6 (4.8%) of our patients.

In terms of follow-up in the 3rd month, 34(27%) of the patients had passed away, 90(71.4%) did not experience any seizures, and only 2 (1.6%) developed seizures. At the 6th month follow-up, 44(34.9%) had passed away, 82(65.1%) had no seizures, and there were no reported seizure cases. At the 12th month follow-up, 50(39.7%) had passed away, 75 (59.5%) had no seizures, and1(0.8%) developed seizures.

As shown in Table 2, we discovered a significant association between seizures and anti-epileptic medication, but not between gender, age, stroke type, ACA, MCA,PCA, dyslipidemia, diabetes mellitus, hypertension, or outcome (p=0.367). Instead, we found no significant associations with any of these variables. We discovered by uni-variate logistic regression that men are more likely than women to experience seizures (OR=1.875, p=0.312). The prevalence of seizures varied across different age groups. The highest occurrence was observed in patients aged 46-60 years (57.1%) (OR=3.012, p=0.070). People with diabetes are more likely to experience seizures than people without diabetes (OR=2.232, p=0.173). People with dyslipidemia are more likely to experience seizures than people without the condition (OR=2.782, p=0.162). Seizures were most commonly associated with cortical strokes (78.6%) (p=0.418, OR=2.406), followed by subcortical (14.3%) and cortical/subcortical strokes (7.1%). Table 3 displays the complete odds results.

Table 2:Association of seizures with factors

	Seizures n(%)		P-value
	Yes	No	
Gender			
Male	10(71.4)	64(57.1)	0.306
Female	4(28.6)	48(42.9)	
Age Group			
≤45 years	1(7.1)	14(12.5)	0.141
46-60years	8(57.1)	34(30.4)	
>60 years	5(35.7)	64(57.1)	
Stroke Type			
Cortical	11(78.6)	64(57.1)	
Subcortical	2(14.3)	34(30.4)	0.355
Cortical/Subcortical	1(7.1)	14(12.5)	
Severity of stroke -NIHSS			
Minor	7(50)	25(22.3)	
Moderate	4(28.6)	53(47.3)	0.102
Moderate to Severe	1(7.1)	23(20.5)	
Severe	2(14.3)	11(9.8)	
Anti-Epileptic drug given	8(57.1)	1(0.9)	0.000
Types of stroke			
ACA	1(7.1)	18(16.1)	0.692
MCA	10(71.4)	82(73.2)	1.000
PCA	3(21.4)	15(13.4)	0.421
Vertebrobasilar	1(7.1)	15(13.4)	1.000
Co-morbidities			
Hypertension	10(71.4)	90(80.4)	0.485
DiabetesMellitus	9(64.3)	50(44.6)	0.165
Dyslipidemia	3(21.4)	10(8.9)	0.159
Outcome			
Alive	10(71.4)	66(58.9)	0.367
Expired	4(28.6)	46(41.1)	

As shown in Table 4, we discovered a statistically significant association between age (p=0.000) and stroke severity as measured by the NIHSS (p=0.002).According to uni-variate logistic regression, males are less likely to die than females (OR=0.951, p=0.893), but patients who have seizures are more likely to die than patients without seizures(OR=1.742,p=0.372). Table 5 shows the odds for expired patients in more detail.

Table 3:Odds ratio for seizures

	p-value	Oddsratio (95%CI)
Gender		
Male	0.312	1.875(0.554-6.341)
Female®		1
Age Group		
≤45years	0.937	0.914(0.099-8.448)
46-60years	0.070	3.012(0.914-9.922)
>60years®		1
Stroke Type		
Cortical	0.418	2.406(0.287-20.192)
Subcortical	0.878	0.824(0.069-9.832)
Cortical/Subcortical®		1
Severity of stroke -NIHSS		
Minor	0.624	1.540(0.275-8.635)
Moderate	0.343	0.415(0.067-2.555)
ModeratetoSevere	0.263	0.239(0.020-2.930)
Severe®		1
Anti-Epileptic Drug given		
Yes	0.000	148.00(15.830-1383.671)
No®		1
ACA		
Present	0.394	0.402(0.049-3.266)
Absent®		1
MCA		
Present	0.887	0.915(0.267-3.137)
Absent®		1
PCA		
Present	0.423	1.764(0.440-7.064)
Absent®		1
Vertebrobasilar		
Present	0.516	0.497(0.061-4.084)
Absent®		1
Hypertension		
Present	0.440	0.611(0.175-2.132)
Absent		1
Diabetes Mellitus		
Present	0.173	2.232(0.703-7.084)
Absent®		1
Dyslipidemia		
Present	0.162	2.782(0.664-11.651)
Absent®		1
Outcome		
Alive	0.372	1.742(0.515-5.897)
Expired®		1

®Reference group

Table 4: Association of outcome with factors

Outcome			**p-value**
	Alive	**Expired**	
Gender			
Male	45(59.2)	29(58)	0.893
Female	31(40.8)	21(42)	
Age Group			
≤45years	11(14.5)	4(8)	0.000
46-60years	34(44.7)	8(16)	
>60years	31(40.8)	38(76)	
Stroke Type			
Cortical	48(63.2)	27(54)	0.221
Subcortical	22(28.9)	14(28)	
Cortical/Subcortical	6(7.9)	9(18)	
Severity of stroke -NIHSS			
Minor	26(34.2)	6(12)	0.002
Moderate	35(46.1)	22(44)	
ModeratetoSevere	12(15.8)	12(24)	
Severe	3(3.9)	10(20)	
Anti-EpilepticDruggiven	6(7.9)	3(6)	1.000
ACA	14(18.4)	5(10)	0.196
MCA	52(68.4)	40(80)	0.152
PCA	13(17.1)	5(10)	0.265
Vertebrobasilar	8(10.5)	8(16)	0.367
Hypertension	61(80.3)	39(78)	0.759
Diabetes Mellitus	37(48.7)	22(44)	0.606
Dyslipidemia	7(9.2)	6(12)	0.615
Seizure	10(13.2)	4(8)	0.367

Table 5:Odds ratio for outcome

	p-value	Odds Ratio (95%CI)
Gender		
Male	0.893	0.951(0.461-1.963)
Female®		1
Age Group		
≤45years	0.055	0.297(0.086-1.024)
46-60years	0.000	0.192(0.078-0.474)
>60years®		1
Stroke Type		
Cortical	0.090	0.375(0.120-1.167)
SubCortical	0.172	0.424(0.124-1.453)
Cortical/Subcortical®		1
Severityof stroke -NIHSS		
Minor	0.001	0.069(0.014-0.331)
Moderate	0.019	0.189(0.047-0.762)
ModeratetoSevere	0.120	0.300(0.066-1.369)
Severe®		1
Anti-EpilepticDruggiven		
Yes	0.687	0.745(0.177-3.125)
No®		1
ACA		
Present	0.203	0.492(0.165-1.465)
Absent®		1
MCA		
Present	0.155	1.846(0.793-4.298)
Absent®		1
PCA		
Present	0.270	0.538(0.179-1.618)
Absent®		1
Vertebrobasilar		
Present	0.370	1.619(0.565-4.639)
Absent®		1
Hypertension		
Present	0.759	0.872(0.363-2.093)
Absent®		1
Diabetes Mellitus		
Present	0.606	0.828(0.404-1.696)
Absent®		1
Dyslipidemia		
Present	0.615	1.344(0.424-4.263)
Absent®		1
Seizure		
Yes	0.372	1.742(0.515-5.897)
No® ®Reference group		1

DISCUSSION

Thromboembolic vascular disease is a frequent precipitant of seizures, and is the most common etiology in older patients[16]. Post-stroke seizures are a serious complication and their frequency varies in different parts of the world. Several prospective and retrospective studies have looked at the frequency and characteristics of post-stroke seizures after an acute ischemic stroke, bringing new insights into this phenomenon. Studies have found varied incidences of post-stroke seizures after an acute ischemic stroke. In the study done by[6], the overall seizure incidence was 8.9%, with10.6% for hemorrhagic stroke and 8.6% for ischemic stroke. Similarly[17], reportedaseizureincidenceof8% among first-time ischemic stroke patients. These results are nearly the same as observed in our study.However, a study done by [18] reported a cumulative incidence of post-stroke epilepsy of 2.5% among acute stroke patients.

Research has looked into the timing of seizures following a stroke. According to one study, 90% of early-onset seizures occurred within 24 hours of the infarction, whereas late-onset seizures occurred afterwards. This conclusion is consistent with our research that out of the 14 patients with seizures, 85.7% experienced early-onset seizures, while 14.3% had late-onset seizures[19]. Furthermore, another similar study done in Pakistan found that 66% of acute symptomatic seizures occurred during the first 24 hours of stroke onset[20]. These findings emphasize the

significance of regularly monitoring patients during the initial period of stroke recovery to detect early seizures.

In terms of seizure types, partial seizures were the most prevalent (71.4%), and our study's findings are similar to the findings of earlier studies[11,19]. One study, however, has found a larger proportion of generalized seizures. This variation could be attributed to differences in the study population, methodology, and seizure classification criteria. These studies also found that early seizures were primarily generalized tonic-clonic, but late seizures were mostly partial with or without subsequent generalization. A French study reported that89% of thepost-stroke seizures were partial seizures and about a third of these patients had secondarily generalized seizures[11]. A Chinese study reports that partial seizures were more frequent in early onset (56%) while generalized seizures were more common in the late-onset group (72%)[17,19].

The use of anti-epileptic drugs (AED) is another factor that has been assessed in this study. According to a study, there are no accepted guidelines to support the prophylactic use of AEDs in ischemic stroke. The use of phenytoin causes more complications in people who used AEDs prophylactically compared to those who did not. Therefore, prophylactic use of AEDs can also cause drug-to-drug interactions in people who are on post-stroke management and can do more harm than good. That is why we discouraged the use of prophylactic anti-epileptic drugs in the management of stroke[20]. Electroencephalography (EEG) findings have also been explored about post-stroke seizures and have been non-consistent throughout the literature. The generalized slow waves were the most prevalent EEG abnormality in patients with post-stroke seizures, which is consistent with our study's results of widespread slowing in 66.7% of cases. However, some other studies have found focal slowing and epileptiform discharges to be linked with post-stroke seizures and especially certain other patterns like PLEDS (periodic lateralized epileptic form discharges) and FIRDA (frontal intermittent rhythmic delta) which cannot be seen in our study[21]. These EEG findings provide additional evidence of the relationship between seizures and the underlying cerebral pathology. EEG was performed in limited cases in our study due to the lack of financial support and its limited utility as a screening tool.

It has been discovered that the type of stroke and its location inside the brain increases the likelihood of post-stroke seizures. Cortical involvement has been reported as a critically important predictor of post-stroke seizures in prior literature especially those ischemic strokes which have a hemorrhagic component with the ischemic core. Thereasonisthatinacuteischemicstroke,there is a concurrent reperfusion of specific brain regions that act as irritants and trigger seizures.[10]We made a comparison group in our study which did not show statistically significant differences in groups with or without seizures. Further large, longitudinal studies are required to establish its significance in our population.

Comparing the results of this study with findings from other studies reveals both similarities and differences in the incidence, risk factors, seizure types, and EEG findings associated with post-stroke seizures. The present study's results corroborate the association between hemorrhagic stroke, cortical involvement, and increased seizure risk. However, variations in seizure incidence rates and types of seizures highlight the heterogeneity of patient populations and the need for further research to better understand the underlying mechanisms and optimize the management of post-stroke seizures.

The study at hand presents certain limitations that merit consideration. First and foremost, the sample size utilized in this research is relatively small, raising questions about the generalizability and statistical power of the findings. Furthermore, the study's follow-up period was confined to a year, potentially missing out on valuable insights regarding the longer-term implications of the variables under investigation. It is also essential to acknowledge that attrition from the study was largely a consequence of patient mortality, which might introduce biases into the dataset. Finally, a lingering concern is thepotentialfor recallbias in datacollection, wherein participants may not accurately recall or report their experiences, affecting the study's overall integrity. These limitations underscore the need for caution when interpreting and extrapolating the study's results.

CONCLUSION

The reported occurrence of post-stroke seizures in our study is in line with what has been described in earlier research conducted on a global scale. Notably, our study identified a higher prevalence of early-onset seizures, with partial seizures being more common than generalized seizures in our findings.

Authorship and contribution declaration: Each author of this article fulfilled following Criteria of Authorship:

1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.

All authors agree to be responsible for all aspects of their research work.

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