Pakistan Journal of Neurological Sciences (PJNS)

Volume 17 | Issue 3 Article 7

9-2022

Predictors of Early Seizures After First Acute Stroke

Malik Muhammad Adil
.Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Sumaira Nabi
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Maryam Khalil
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Zeeshan Munawar
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Nayab Aslam
Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan

See next page for additional authors

Predictors of Early Seizures After First Acute Stroke

Authors

Malik Muhammad Adil, Sumaira Nabi, Maryam Khalil, Zeeshan Munawar, Nayab Aslam, and Zaid Waqar

https://doi.org/10.56310/pjns.v17i03.196

PREDICTORS OF EARLY SEIZURES AFTER FIRST ACUTE STROKE

Malik Muhammad Adil[1], Sumaira Nabi[1], Maryam Khalil[1], Zeeshan Munawar[1], Nayab Aslam[2], Zaid Waqar[1]
[1].Pakistan Institute of Medical Sciences, Islamabad, Pakistan
[2].Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan

Corresponding author: Malik Muhammad Adil, Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad, Pakistan **Email:** dr.adil31@gmail.com

Date of submission: August 16, 2022 **Date of revision:** September 24, 2022 **Date of acceptance:** September 24, 2022

ABSTRACT

Background and objective:
There is a lack of local data regarding the frequency and predictors of early seizures after stroke. The objective of this study was to determine the frequency of early seizures after stroke and identify the predictors which lead to them after first acute stroke.

Methods:
This cross-sectional observational study was conducted in the Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad from October 2021 to June 2022. A total of 310 consecutive eligible patients of acute stroke were recruited. Key inclusion criteria included any patient of >20 years of age with confirmed diagnosis of stroke on imaging, non-traumatic, with no history of seizures in past. Data was analyzed by SPSS version 23.0.

Results:
The mean age of patients in the seizures group was 48.40 ± 20.9 years. Hypertension was the most common co-morbid present in 225 (76.5%) patients. Early seizures were found in 52 (16.8%) patients with 42 (80.76%) having seizures in first 24 hours of stroke (p value 0.001). On National Institute of Health Sciences Scale (NIHSS) score most patients 125 (40.3%) had moderate severity score i.e. score in between 7 to 25 (p value 0.05). Ischemic stroke was identified as the stroke variety with most of the early seizures i.e. 16 (30.76%) (p value 0.003).

Conclusion: Early seizures were not infrequent after acute stroke (16.77%) in our study. Early seizures were associated with younger age, cortical region lesion, ischemic stroke, followed by cerebral venous thrombosis. Higher NIHSS score and greater disability was associated with increased incidence of early seizures.

Key words: Acute stroke, Early seizures, Stroke score, Ischemic stroke, Hemorrhagic stroke, Hemorrhagic ischemic stroke, Cerebral venous sinus thrombosis

INTRODUCTION

Any acute brain insult like stroke, traumatic brain injury and cerebral infections may cause seizures.[1] Stroke is defined as the sudden development of neurological deficit due to acute loss of blood supply to a part of the brain.It can be hemorrhagic or ischemic depending upon the cause which leads to brain flow compromise. About 4-14% patients of acute intra cerebral hemorrhage suffer from seizures as reported in literature.[3] Reportedly, stroke is a common condition which causes epilepsy in adults. Overall acute stroke leads to status epileptics in about 22% adult patients.[4] Classically, post-stroke seizures are classified as early and late onset seizures. Early or acute symptomatic seizures are those which occur at the time of brain injury and they indicate the severity of brain injury and affect the outcome in terms of morbidity and mortality.[1] Early seizures (ES) are defined as seizures which occur in 24 hours to 30 days of stroke and are reported in about 2% to 6% patients of acute stroke.[4] Risk factors for early seizures are stroke severity, intracerebral hemorrhage (ICH), lobar hematoma and young age.[3] Late seizures are those which occur after 30 days and their reported rate is 3% to 7.3%.5A series of biological events in the injured brain tissue lead to late onset seizures and epilepsy. Risk factors which

lead to late onset seizures are cortical involvement, previous history of dementia, young age and cerebral amyloid angiopathy.[6]

Elderly patients are more likely to develop seizures after stroke, particularly in those who develop a brain lesion and are more prone to recurrent seizures than their young counterparts.[7] So the first seizures reported after stroke should be carefully sorted out to identify the factors and to establish a lower threshold for subsequent seizures. A study by Fischer et al showed that a person who experiences a first seizure after stroke has about 60 % chances of recurrence.[8] It is also reported in literature that irrespective of type of stroke, the incidence of seizures is the same.[9]

This study was conducted to provide data on the frequency of early seizures following an acute stroke in Pakistan and to identify high risk individuals to reduce further seizures in the future. There is little local data available in this context.It will also help in the proper management of these patients which will in turn affect their long-term quality of life.

METHODS

Study design: Cross-sectional observational study

Place and duration of study: This study was conducted in the Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad from October 2021 to June 2022 after approval from the ethical committee.

Sample size: A sample size of 310 patients was calculated by keeping 80% power of study, 5% significance level and frequency of early onset seizures i.e. 40.9%.

Sampling technique: Non-probability consecutive sampling.

Inclusion criteria: Any patient>20 years of age with confirmed diagnosis of stroke both clinically and on imaging (CT scan brain without contrast, MRI brain Stroke Protocol or MRV in cases of CVST), non-traumatic, with no history of seizures in the past.

Exclusion criteria: Patients of hepatic or renal failure, patients having metabolic disorders, hypoglycemia or hyperglycemia and electrolyte imbalance, and drug addicts

Data collection: Consecutive patients were included in the study after diagnosis of stroke was confirmed on CT scan or MRI. All types of Stroke variety were included- arterial (ischemic and hemorrhagic) as well as venous. Informed written consent was taken from all patients or their relatives. Data was recorded on proforma by postgraduate trainees on duty. Patients were followed till the time of discharge and findings were noted. Seizures were divided into three categories i.e. early onset seizures (occurring within 24 hours), within 7 days and late onset seizures (occurring after 7 days). Seizures were observed and classified into focal seizures and generalized seizures. EEG was done in patients who developed seizures. Antiepileptic drugs were given accordingly. Patients of ischemic stroke were treated conservatively (as tPA was not available at the hospital). The severity of stroke was assessed using National Institute of Health Stroke Scale (NIHSS).11 According to NIHSS patients were categorized as; score < 7 as mild, score 7-25 as moderate and >25 as severe. Patients were broadly divided into two groups, i.e. group A comprised of patients who experienced seizures and group B of patients with absence of seizures and then different variables were compared in both groups.

Data analysis: Data was entered and analyzed in SPSS version 23.0. Mean and standard deviation were calculated for quantitative variables and frequency and percentages for qualitative variables. Chi-Square test was used and P value <0.05 was considered as significant.

RESULTS

A total number of 310 consecutive patients of acute stroke were included in the study. The mean age of patients was 57.05 ± 1.60years. There were 156 (50.3%) males and 154 (49.7%) females. It was seen that patients in whom seizures had occurred were younger than those in the non-seizure group i.e. mean age of patients in seizures group was 48.40 ± 20.9 and in non-seizure group it was 58.80 ± 14.24 which was statistically significant(p value 0.001). Hypertension was the most common comorbid present in 225 (76.5%), and in 32 patients (61.53%) of seizure group (p value 0.001), followed by ischemic heart disease which was present in 91 (29.4%) patients. One-hundred-twenty-five (40.3%) patients included in the study had ischemic stroke in cortical region followed by hemorrhagic stroke in cortical region which was present in 93 (30.0%) patients (p value 0.003). Other comorbids and patients demographics are mentioned in Table 1.

Table 1: Demographics

Variable	n %	Seizures	Non seizures	P value
No of patients	310	52	258	
Age (years)	57.05 ± 1.60	48.40 ± 20.9	58.80 ± 14.24	0.001
Male	156 (50.3%)	24(15.38%)	132(84.62%)	-
Female	154 (49.7%)	28(18.18%)	126(81.82%)	-
Hypertension	225 (76.5%)	32(14.22%)	193(83.78%)	0.05
Diabetes Mellitus	84 (27.1%)	6(7.14%)	78(92.86%)	0.006
Ischemic Heart Disease	91 (29.4%)	18(19.78%)	73(80.22%)	0.3
Ischemic stroke (cortical)	125 (40.3%)	20(16%)	105(84%)	0.003
Ischemic stroke (Brainstem)	22 (7.1%)	2(11%)	20(89%)	
Ischemic with hemorrhagic transformation(Cortical)	26 (8.4%)	2(13%)	24(87%)	
Hemorrhagic stroke (cortical)	93 (30.0%)	9(9.6%)	84(90.4%)	
Hemorrhagic stroke (Brainstem)	20 (6.5%)	5 (25%)	15(75%)	
CVST	24 (7.7%)	14(58.33%)	10(41.66%)	

CVST: Cerebral venous sinus thrombosis

Early seizures were found in 52 (16.8%) patients with 42 (80.76%) patients having seizures in the first 24 hours of stroke(p value 0.001) and 10(28.6%) patients have seizures in 7 days of stroke (p value 0.001). Generalized seizures were present in 26 (50%) patients followed by focal seizures which were present in 20 (38.46%) patients (p value 0.001). Most common EEG findings were generalized spike and wave discharges which were present in 20 (38.46%) patients (p value 0.00). Forty-eight (92.3%) patients responded to single antiepileptic drug and multiple antiepileptic drugs were used in only 4 (7.7%) patients (p value 0.001). The various characteristics of seizures are mentioned in Table 2.

Table 2: Characteristics of seizures

Variable		n(%)	P value
Early Seizures		52 (16.8%)	-
Time of onset of seizures	< 24 hours	42 (80.76%)	0.001
	Within 7 days	10 (19.24%)	
Type of seizures	Focal	20 (38.5%)	0.001
	Generalized	26 (50%)	
	Focal with generalized	6 (11.5%)	
EEG Findings	Normal	4 (7.7%)	0.000
	Encephalopathic	2 (3.8%)	
	Generalised epileptiform Discharges	20 (38.46%)	
Antiepileptic therapy	Monotherapy	48 (92.3%)	0.001
	Polytherapy	4(7.7%)	

CT scan was most commonly used imaging modality and was done in 260 (83.9%) patients. Findings of the CT scan suggested that large vessels were most commonly involved in stroke patients i.e. in 93 (30%) patients. On the NIHSS it was observed that 125 (40.3%) had moderate severity score in between 7 to 25 (p value 0.05). Table 3 summarizes these findings.

Table 3: Radiological and NIHSS findings

Variable		n (%)	P value
Imaging Modality	CT Scan brain (plain)	260 (83.9%)	-
	Both CT scan and MRI brain (stroke protocol)	50 (15.1%)	
Radiological Findings	Supratentorial lesion	67 (21.6%)	0.1
	Infratentorial lesion	38 (12.3%)	
	Small Vessel stroke	19 (6.1%)	
	Medium Vessel stroke	93 (30%)	
	Large Vessel stroke	93 (30%)	
NIHSS	Mild severity	99 (31.9%)	0.05
	Moderate severity	125 (40.3%)	
	Severe	86 (27.7%)	

NIHSS: National Institute of Health Sciences Scale

When the time of onset seizures was compared it was seen that ischemic stroke was responsible for most of the early seizures i-e 16 (30.76%) patients had early seizures in 24 hours and six (11.53%) patients had seizures in seven days of stroke. Although generalized seizures were most commonly found overall, focal seizures were most commonly present in patients of ischemic stroke i.e. 12 (60%). thriteen (65%) patients of ischemic stroke had epileptiform waveform on EEG. Sixty-six patients (52.8%) of ischemic stroke had moderate severity score on NIHSS. Table 4 summarizes these findings.

Table 4: Comparison of variables in different types of stroke

Variable	IS	**HIS**	**HS**	**CVST**	**Total**
Time of seizures					
< 24 hours	16(37.1%)	2 (4.8%)	12(28.6%)	12(28.6%)	42
Within 7 days	6 (60%)	-	2 (20%)	2 (20%)	10
Type of Seizures					
Focal	12 (60%)	-	6 (30%)	2 (10%)	20
Generalized	6 (23.1%)	2 (7.7%)	8 (30.8%)	10(38.5%)	26
Focal with generalization	4 (66.6%)	-	-	2 (33.3%)	6
EEG					
Normal	-	2(50%)	2 (50%)	-	4
Encephalopathic	2 (65%)	-	-	-	2
Epileptiform	13 (65%)	-	3 (15%)	4(20%)	20
AED Therapy					
Monotherapy	22(45.9%)	2 (4.1%)	10(20.8%)	14(29.2%)	48
Polytherapy	-	-	4 (100%)	-	4
NIHSS					
Mild	39(39.4%)	4 (4%)	39(39.4%)	17(17.2%)	99
Moderate	66(52.8%)	13(10.4%)	39(31.2%)	7(5.6%)	125
Severe	42(48.8%)	9(10.5%)	35(40.7%)	-	86

IS: Ischemic stroke
HIS: Hemorrhagic ischemic stroke
HS: Hemorrhagic stroke
CVST: Cerebral venous sinus thrombosis
NIHSS: National Institute of Health Sciences Scale

DISCUSSION

Stroke is the most common cause of seizure in adults as reported in literature. The incidence of seizures after stroke is about 10% (5% each of early and late seizures).[12] The Oxfordshire community stroke project (OCSP) reported that 11.5% of stroke patients are at a risk of developing post-stroke seizures by five years.[13] Seizures have been identified as complication of ischemic stroke and they generally worsen the prognosis of stroke and lead to further complications.[14]

In our study post stroke early seizures were seen in 16.77% patients and mostly patients (80.76%) had early seizures in first 24 hours of onset of stroke which was statistically significant. These results are comparable to those shared by Turaga et al which reported early seizures in 11.8% of their patients.[1] Similarly Law et al reported the incidence of post stroke seizures about 8.3% of which early seizures comprised of 84.5% of seizures patients.[3] The incidence of seizures reported by Bryndziar et al was 7.2% with early seizures occuring in 40% patients.[5] Bentes et al reported that early seizures occurred in 15% of their patients.[15] In our study seizures were more commonly seen in younger age group i.e. mean age 48.40 ± 20.9 years. Similar results were shared by Turaga et al who stated that mean age group of seizures patients was 50.9 ± 17.27 years.[1] Law et al stated that younger age and higher NIHSS are associated with early seizures.[3]A meta-analysis by Gasparini et al showed that early seizures were more commonly seen in younger patients as compared to elders.[16] Breitweg et al also reported in their study that early seizures are associated with younger patients and late on may present as late onset epilepsy.[17]

In our study most of the patients with early seizures had NIHSS score in between 7-25 i-e moderate severity. Zöllner et al reported that NIHSS was a good predictor of early onset seizures after stroke and higher the NIHSS higher the chances of early seizures.[18] Moreira et al showed that higher NIHSS was associated with higher rate of early seizures in post stroke patients.[19] Castro-Apolo et al and Lio et al in two different studies also reported that higher the NIHSS more the chances of developing early seizures.[20,21] 20 patients (38.46%) in our study who had early seizures had ischemic stroke in cortical region (p value 0.003). These results are similar to meta-analysis by LEE et al in that cortical involvement, younger age and large area involved were strong factors associate with early seizures.[22] A meta-analysis by Baudin et al showed that early seizures were associated with cortical region lesions, hypertension and low GCS on presentation.[23] Galovic et al and Zelano et al also stated in their studies that early seizures were more likely when cortical region is involved.[24,25]

The limitation of our study is that it only included early seizures and late seizures were not included. Also it does not include patient hospital stay, and further out patient department follow up, which if included will have commented on long term outcomes and help in long term management of patients with early seizures.

CONCLUSION

We conclude that early seizures frequency was quite higher (16.77%) in our study as compared to other similar studies. Early seizures were associated with younger age, cortical region lesion, ischemic stroke, followed by cerebral venous thrombosis. The higher NIHSS score and greater disability is associated with increased incidence of early seizures

REFERENCES

1. Turaga SP, Chaithanya RL, Kohat AK, Alladi S, Kaul S. Frequency and Predictors of Early Seizures Following First Acute Stroke: Data from a University Hospital in South India. Neurol India. 2021;69(4):847.
2. Candelario-Jalil E, Paul S. Impact of aging and comorbidities on ischemic stroke outcomes in preclinical animal models: a translational perspective. Exp Neurol. 2021;335:113494.
3. Law ZK, England TJ, Mistri AK, Woodhouse LJ, Cala L, Dineen R,et al. Incidence and predictors of early seizures in intracerebral haemorrhage and the effect of tranexamic acid. Eur Stroke J. 2020;5(2):123-9.
4. Labovitz DL, Hauser WA, Sacco RL. Prevalence and predictors of early seizure and status epilepticus after first stroke. Neurology. 2001;57(2):200-6.
5. Bryndziar T, Sedova P, Kramer NM, Mandrekar J, Mikulik R, Brown Jr RD, et al. Seizures following ischemic stroke: frequency of occurrence and

   impact on outcome in a long-term population-based study. J Stroke Cerebrovasc Dis. 2016;25(1):150-6.
6. Biffi A, Rattani A, Anderson CD, Ayres AM, Gurol EM, Greenberg SM, et al. Delayed seizures after intracerebral haemorrhage. Brain. 2016;139(10):2694-705.
7. Assis T, Bacellar A, Costa G, Pires E, Nascimento O.Predictors of early seizure recurrence among elderly inpatients admitted to a tertiary center: a prospective cohort study. Epilepsy Behav. 2019;98:145-52.
8. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014 ;55(4):475-82.
9. Zhang C, Wang X, Wang Y, Zhang JG, Hu W, Ge M, et al. Risk factors for post-stroke seizures: a systematic review and meta-analysis. Epilepsy Res. 2014;108(10):1806-16.
10. Coupland AP, Thapar A, Qureshi MI, Jenkins H, Davies AH. The definition of stroke. J R Soc Med .2017 ;110(1):9-12.
11. Lyden P. Using the national institutes of health stroke scale: a cautionary tale. Stroke. 2017 Feb;48(2):513-9.
12. Galovic M, Ferreira-Atuesta C, Abraira L, Döhler N, Sinka L, Brigo F, et al. Seizures and epilepsy after stroke: epidemiology, biomarkers and management. Drugs Aging. 2021;38(4):285-99.
13. Jones FJ, Sanches PR, Smith JR, Zafar SF, Blacker D, Hsu J, et al. Seizure Prophylaxis After Spontaneous Intracerebral Hemorrhage. JAMA Neurol.2021;78(9):1128-36.
14. Pande SD, Lwin MT, Kyaw KM, Khine AA, Thant AA, Win MM, et al. Post-stroke seizure—Do the locations, types and managements of stroke matter?. Epilepsia open. 2018 Sep;3(3):392-8.
15. Bentes C, Martins H, Peralta AR, Morgado C, Casimiro C, Franco AC, et al. Early EEG predicts poststroke epilepsy. Epilepsia Open. 2018;3(2):203-12.
16 Gasparini S, Ascoli M, Brigo F, Cianci V, Branca D, Arcudi L, et al. Younger age at stroke onset but not thrombolytic treatment predicts poststroke epilepsy: an updated meta-analysis. Epilepsy Behav. 2020 Mar 1;104:106540.
17. Breitweg I, von Stülpnagel C, Pieper T, Lidzba K, Holthausen H, Staudt M, et al. Early seizures predict the development of epilepsy in children and adolescents with stroke. Eur J Paediatr Neurol.2017;21(3):465-7.
18. Zöllner JP, Misselwitz B, Kaps M, Stein M, Konczalla J, Roth C, et al. National Institutes of Health Stroke Scale (NIHSS) on admission predicts acute symptomatic seizure risk in ischemic stroke: a population-based study involving 135,117 cases. Sci Rep. 2020 Mar 2;10(1):1-7.
19. Moreira MM, Andrade JB, Araújo DS, Rolim FP, Monteira MR, Frota NA, et al. Prevalence, risk factors and prognostic of seizures after ischemic stroke.2022.
20. Castro-Apolo R, Huang JF, Vinan-Vega M, Tatum WO. Outcome and predictive factors in post-stroke seizures: a retrospective case-control study. Seizure. 2018;62:11-6.
21. Liao HC, Chen SH, Yang CD, Chen YW. Clinical

profile and outcomes of early seizures in asian patients with acute intracerebral hemorrhage. J Acute Med. 2019;9(4):172.
22. Lee SH, Aw KL, Banik S, Myint PK. Post-stroke seizure risk prediction models: a systematic review and meta-analysis. Epileptic Disord. 2022 ;24(2):302-14.
23. Baudin P, Cousyn L, Navarro V. The LGI1 protein: molecular structure, physiological functions and disruption-related seizures. Cell Mol Life Sci. 2022;79(1):1-7.
24. Galovic M, Döhler N, Erdélyi-Canavese B, Felbecker A, Siebel P, Conrad J, et al. Prediction of late seizures after ischaemic stroke with a novel prognostic model (the SeLECT score): a multivariable prediction model development and validation study. Lancet Neurol. 2018;17(2):143-52.
25. Zelano J, Holtkamp M, Agarwal N, Lattanzi S, Trinka E, Brigo F. How to diagnose and treat post-stroke seizures and epilepsy. Epileptic Disord. 2020;22(3):252-63.

Conflict of interest: Author declares no conflict of interest.
Funding disclosure: Nil

Author's contribution:
Malik Muhammad Adil; concept, data collection, data analysis, manuscript writing, manuscript review
Sumaira Nabi; data collection, data analysis, manuscript writing, manuscript review
Maryam Khalil; concept, data analysis, manuscript review
Zeeshan Munawar; data collection, data analysis, manuscript writing
Nayab Aslam; data collection, data analysis, manuscript writing
Zaid Waqar; concept, manuscript review