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Stroke-related early seizures: clinical and neurophysiological study in a sample of Egyptian population

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Abstract

Background: Available data collected from patients of different types of acute cerebrovascular strokes can detect risk factors, clinical data (including semiology of seizures), EEG findings and functional outcome of these patients. Stroke, both ischemic and hemorrhagic, has been considered an essential cause of epilepsy, especially in the elderly. Complications of acute stroke during the early days after the insult determine the ultimate outcome of events. The aim of this study is to determine the clinical and neurophysiological characteristics of stroke patients with or without clinical evident fits for early detection and better management.

Results: The brain imaging of the cases group who developed seizures showed that 50% of the cases have arterial ischemic infarction, 30% venous infarction, 6.67% ischemic infarction with haemorrhagic transformation, 6.67% intracerebral haemorrhage and 6.67% have subarachnoid haemorrhage. Based on the 2017 ILAE criteria, 43.33% of the patients developed focal to bilateral tonic clonic seizures, 33.33% developed focal aware seizures, 16.67% of the patients developed generalized tonic clonic seizures and 6.67% of the patient developed status epilepticus. EEG findings of the group of patients who developed seizures showed, focal slowing in 46.67%, focal epileptiform activity in 13.33%, focal activity with secondary generalization in 10%, PLEDS in 6.67%, generalized epileptiform activity in 6.67%, generalized slowing in 6.67% and normal EEG in 10% of the patients. Non convulsive status was found in 2 patients (6.67%) of the group with altered mental status. There was no PLEDS in EEG of group of patients without clinical seizures. This study did not find age and sex differences in patients with and without seizures. In addition, it was found that there was no statistically significant difference between the three groups as regard history of diabetes mellitus, hypertension, heart diseases, atrial fibrillation, carotid stenosis and collagen diseases. There was no significant relationship between seizures and early treatment with Rtpa and thrombectomy.

Conclusions: Focal to bilateral tonic clonic and focal aware seizures were the most prevalent type of early onset seizures after stroke, followed by generalized tonic clonic seizures and status epilepticus. Most EEG findings in this study were focal slowing, focal epileptiform activities, generalized epileptiform activities and PLEDS.

Keywords: Epilepsy, Post-stroke seizures, Cerebrovascular stroke, Thrombectomy

Introduction

The most common cause of seizures and epilepsy in older adults is stroke. Seizures immediately after stroke can cause increased metabolic stress and cell death, causing an increase in infarct size, mortality and negative functional outcomes. Recurring seizures may lead to injuries,

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affect cognitive functions and the ability to work or drive and decrease the quality of life [1]. Post stroke seizures (PSS) is classified into early onset and late onset seizures according to the underlying pathological mechanisms. Early onset PSS may result from acute neuron injury, glutamate-mediated excitotoxicity, ion channel dysfunction and interruption of blood barrier [2]. EEG is the optimum diagnostic tool after cerebral ischemic or hemorrhagic injuries, for assessing the electrical activity and functional state of the brain, providing for the diagnosis of non-convulsive seizures and predicting the disease outcome [3]. Many studies were conducted on the late onset seizures after stroke lacking the characteristics of the early post stroke seizures including different types of bleeding and intracranial venous thrombosis. The aim of this study is to determine the clinical and neurophysiological characteristics of stroke patients with or without clinical evident fits for early detection and better management.

Methods

Ninety patients were recruited from the stroke unit of the University hospital from August 2020 through May 2022. Sample size was calculated using open epi, version 3 open source calculator and based on a study carried out by wolf et al., 2016. A written informed consent was obtained from all participants and the study was approved by local research ethics committee FWA 000017585 in 2020. All procedures performed in the study were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This is an observational cross-sectional study with a convenient sample. The study recruited 90 patients divided into 3 groups, 30 acute stroke patients with seizures, 30 acute stroke patients with altered mental status and 30 acute stroke patients without epileptic phenomenon. All patients were above 18 years of age. Patients were included in the first group if they had symptomatic seizures, they were included in second group if they had altered mental status and patients without epileptic phenomenon were included in third group. Patients were excluded if they had previous CVS with mRS > 1, brain imaging with (brain contusion, subdural hemorrhage, extradural hemorrhage, neoplastic lesion, inflammatory or infectious lesion), previous head trauma with hospital admission, previous neurosurgery, previous history of epilepsy. All patients were subjected to complete history including personal data, family history of epilepsy, past history and risk factors, detailed history of current illness, complete clinical picture, semiology of seizures and drug history, general and neurological examination. Stroke severity was assessed by National Institutes of Health Stroke Scale on admission and the modified

Rankin Scale (mRS) was assessed on discharge to detect functional outcome. All patients underwent laboratory investigations (random blood sugar, CBC, liver functions, kidney functions and serum electrolytes). CT brain and/or MRI stroke protocol was performed, to investigate type, site and size of CVS. All patients underwent digital electroencephalogram (EEG) for at least 1 h.

Statistical analysis

Data analysis was done using IBM SPSS software package version 25.0 (Armonk, NY: IBM Corp). Descriptive data were described in Mean, Standard deviation (\pm SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data. Frequency and percentage of non-numerical data, while analytical data were described in ANOVA test was used to assess the statistical significance of the difference between more than two study group means, The Kruskal–Wallis test was used to assess the statistical significance of the difference between more than two study group ordinal variables, Post Hoc Test is used for comparisons of all possible pairs of group means, chi-square test was used to examine the relationship between two qualitative variables and the Fisher's exact test was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells. The significance of the obtained results was judged at $P < 0.05$.

Results

The mean age of the group without seizures or DCL is 59.07 ± 11.29 , while it was 61.07 ± 14.01 and 53.23 ± 14.01 in the group with DCL and the group with seizures, respectively. There was no statistically significant difference between three groups as regard the age and sex. Moreover, there was no significant difference between groups as regards risk factors (diabetes mellitus, hypertension, heart diseases, atrial fibrillation, collagen diseases and carotid stenosis) except smoking (Table 1).

According to 2017 ILAE classification system, 43.33% of the patients developed focal onset to bilateral tonic clonic seizures, 33.33% developed focal onset aware seizures, 16.67% of the patients developed generalized onset tonic clonic seizures, 6.67% of the patient developed status epilepticus (Table 2).

The brain imaging of the stroke group who developed seizures showed that, 50% of them had arterial ischemic infarction, 30% had venous infarction, 6.67% had ischemic infarction with haemorrhagic transformation, 6.67% had intracerebral haemorrhage and 6.67% had subarachnoid haemorrhage. The incidence of seizures was higher for the patients with PACS (33.33%), than TACS (13.33%), PCS (10%) and lacunar syndrome

Table 1 Demographic data and risk factors

| | Group | | | Test of significance | | |
|------------------|--------------------|--------------------|--------------------|----------------------|---------|-----|
| | Control | DCL | Fits | Value | p value | Sig |
| | Mean ± SD N (%) | Mean ± SD N (%) | Mean ± SD N (%) | | | |
| Age | 59.07 ± 11.29 | 61.07 ± 14.01 | 53.23 ± 14.01 | <i>f</i> = 2.867 | 0.062 | NS |
| Sex | | | | | | |
| Male | 18 (60%) | 11 (36.67%) | 13 (43.33%) | $\chi^2 = 3.482$ | 0.175 | NS |
| Female | 12 (40%) | 19 (63.33%) | 17 (56.67%) | | | |
| smoking | | | | | | |
| No | 17 (56.67%) | 27 (90%) | 22 (73.33%) | $\chi^2 = 8.532$ | 0.014 | S |
| Yes | 13 (43.33%) | 3 (10%) | 8 (26.67%) | | | |
| DM | | | | | | |
| No | 18 (60%) | 19 (63.33%) | 21 (70%) | $\chi^2 = 0.679$ | 0.712 | NS |
| Yes | 12 (40%) | 11 (36.67%) | 9 (30%) | | | |
| HTN | | | | | | |
| No | 9 (30%) | 6 (20%) | 13 (43.33%) | $\chi^2 = 3.836$ | 0.147 | NS |
| Yes | 21 (70%) | 24 (80%) | 17 (56.67%) | | | |
| Heart disease | | | | | | |
| No | 19 (63.33%) | 21 (70%) | 20 (66.67%) | Fisher's Exact test | 0.336 | NS |
| Ischemic | 8 (26.67%) | 9 (30%) | 10 (33.33%) | | | |
| Rheumatic | 3 (10%) | 0 (0%) | 0 (0%) | | | |
| AF | | | | | | |
| No | 23 (76.67%) | 23 (76.67%) | 26 (86.67%) | $\chi^2 = 1.25$ | 0.535 | NS |
| Yes | 7 (23.33%) | 7 (23.33%) | 4 (13.33%) | | | |
| Collagen ds | | | | | | |
| No | 28 (93.33%) | 29 (96.67%) | 28 (93.33%) | Fisher's Exact test | 1.00 | NS |
| Yes | 2 (6.67%) | 1 (3.33%) | 2 (6.67%) | | | |
| Carotid stenosis | | | | | | |
| No | 29 (96.67%) | 26 (86.67%) | 28 (93.33%) | Fisher's Exact test | 0.493 | NS |
| Yes | 1 (3.33%) | 4 (13.33%) | 2 (6.67%) | | | |

DM: diabetes mellitus, HTN: hypertension, AF: atrial fibrillation, DCL: disturbed conscious level

One Way ANOVA test of significance (*f*)

Chi-square test of significance (χ^2)

Table 2 Type of seizures in the stroke group with seizures

| | Seizures N (%) |
|---|-------------------|
| Type of seizures | |
| No | 0 (0%) |
| Generalized onset, non-motor (Absence) | 0 (0%) |
| Focal onset seizures, aware | 10 (33.33%) |
| Generalized onset, motor (tonic-clonic) | 5 (16.67%) |
| Focal onset to bilateral tonic clonic | 13 (43.33%) |
| Status epilepticus | 2 (6.67%) |

(0%) according to OCSP classification. There was no statistically significant difference between the three groups as regard the site of stroke ($p > 0.05$) (Table 3).

EEG showed focal slowing in (60% of control group, 46.67% of seizures group and 40% of DCL group), focal epileptiform activity in (13.33% of seizures group), focal activity with secondary generalization in (10% in seizures group and 3.33% of DCL group), PLEDS in (6.67% of seizures group), generalized epileptiform activity in (6.67% of seizures group), generalized slowing in (40% of DCL group and 6.67% of seizures group) and normal EEG in (40% of control group, 10% of the patients with DCL and seizures). Non convulsive status was found in 2 patients (6.67%) of the group with DCL (Table 4).

There was no significant relationship between seizures and early treatment with Rtpa and thrombectomy, only 2 patients received Rtpa in the group who developed clinical seizures and 1 patient underwent mechanical thrombectomy ($p > 0.05$) (Table 5).

Table 3 Type, site and size of stroke in the three groups

| | Group | | | Fisher's Exact test | |
|--|-------------|-------------|-------------|---------------------|-----|
| | Control | DCL | Fits | p value | Sig |
| | N (%) | N (%) | N (%) | | |
| Haemorrhagic stroke | | | | | |
| No | 26 (86.67%) | 20 (66.67%) | 26 (86.67%) | 0.296 | NS |
| Intracranial | 3 (10%) | 6 (20%) | 2 (6.67%) | | |
| Subarachnoid | 1 (3.33%) | 4 (13.33%) | 2 (6.67%) | | |
| Ischemic stroke | | | | | |
| No | 4 (13.33%) | 9 (30%) | 4 (13.33%) | 0.01 | S |
| Arterial infarction | 23 (76.67%) | 15 (50%) | 15 (50%) | | |
| Venous infarction | 2 (6.67%) | 1 (3.33%) | 9 (30%) | | |
| Ischemic infarction with haemorrhagic transformation | 1 (3.33%) | 5 (16.67%) | 2 (6.67%) | | |
| Site of stroke | | | | | |
| No | 2 (6.67%) | 3 (10%) | 4 (13.33%) | 0.41 | NS |
| Cortical | 25 (83.33%) | 24 (80%) | 26 (86.67%) | | |
| Non-cortical | 3 (10%) | 3 (10%) | 0 (0%) | | |
| Size (OCSP) | | | | | |
| None | 6 (20%) | 10 (33.33%) | 13 (43.33%) | 0.154 | NS |
| Lacunar syndrome | 4 (13.33%) | 0 (0%) | 0 (0%) | | |
| Partial anterior circulation syndrome (PACS) | 7 (23.33%) | 7 (23.33%) | 10 (33.33%) | | |
| Total anterior circulation syndrome (TACS) | 7 (23.33%) | 8 (26.67%) | 4 (13.33%) | | |
| Posterior circulation syndrome (PCS) | 6 (20%) | 5 (16.67%) | 3 (10%) | | |

OCSP: oxfordshire community stroke project; DCL: disturbed conscious level

Table 4 Comparison of EEG findings between the three groups

| | Group | | | Fisher's Exact test | |
|-----------------------------------|----------|-----------|-------------|---------------------|-----|
| | Control | DCL | Fits | p value | Sig |
| | N (%) | N (%) | N (%) | | |
| EEG | | | | | |
| Normal | 12 (40%) | 3 (10%) | 3 (10%) | <0.001 | S |
| Focal epileptiform activity | 0 (0%) | 0 (0%) | 4 (13.33%) | | |
| Generalized epileptiform activity | 0 (0%) | 0 (0%) | 2 (6.67%) | | |
| Focal with 2ry generalization | 0 (0%) | 1 (3.33%) | 3 (10%) | | |
| Focal slowing | 18 (60%) | 12 (40%) | 14 (46.67%) | | |
| Generalized slowing | 0 (0%) | 12 (40%) | 2 (6.67%) | | |
| PLEDS | 0 (0%) | 0 (0%) | 2 (6.67%) | | |
| Non-convulsive status | 0 (0%) | 2 (6.67%) | 0 (0%) | | |

EEG: electroencephalogram, PLEDS: periodic lateralized epileptic discharges, DCL: disturbed conscious level

Levetiracetam was given to 76.67% and 23.33% of the group with seizures and the group with DCL, respectively, while oxycarbazepine was given to 20% and 3.33% of the group with seizures and the group with DCL, respectively. However, phenytoin was given 3.33% to the group with seizures and the group with DCL. Valproate was given to 16.67% of the group with seizures.

Occurrence of early seizures was not a risk factor for poor functional outcome at discharge from hospital. There was no statistically significant difference between the three groups as regard the functional outcome ($p > 0.05$) (Table 6).

Table 5 Type of treatments the stroke patients received on admission to stroke unit

| | Group | | | Test of significance | | |
|------------------------|-------------|-------------|-----------|----------------------|---------|-----|
| | Control | DCL | Fits | Value | p value | Sig |
| | N (%) | N (%) | N (%) | | | |
| Treatment on admission | | | | | | |
| None | 20 (66.67%) | 25 (83.33%) | 27 (90%) | Fisher's Exact test | 0.118 | NS |
| Rtpa | 9 (30%) | 4 (13.33%) | 2 (6.67%) | | | |
| Thrombectomy | 1 (3.33%) | 1 (3.33%) | 1 (3.33%) | | | |

Rtpa: recombinant tissue plasminogen activator; DCL: disturbed conscious level

Discussion

This study found that there was no statistically significant difference in age and sex between cases and controls. In agreement with a study did not find age differences in patients with and without seizures [4]. This result may be explained by the small sample size. In contrast to a study determined that having stroke younger than 65 years was an important risk factor for seizure occurrence [2].

This study was in agreement with a study found that, both genders have the same risk of post stroke seizures [5]. In contrast to a study found that, post-stroke seizures were more common in male patients than females [6]. Another study found that the female gender is associated with a higher risk of early seizures after stroke [7].

This study found that there was no statistically significant difference between the three groups as regard history of diabetes mellitus, hypertension, heart diseases, atrial fibrillation, carotid stenosis and collagen diseases. In agreement with a study found that the above factors have no obvious relationship with the occurrence of early seizures [8]. In contrast to a study showed that there is a high correlation between hypertension, diabetes mellitus, heart diseases and the occurrence of early seizures [9].

This study found that 43.33% of the patients developed focal to bilateral tonic clonic seizures, 33.33% developed focal aware seizures, 16.67% of the patients developed generalized tonic clonic seizures and 6.67% of the patient developed status epilepticus. The same as a study found

that 72% of PSS were focal onset seizures, among them 22% with evolution on bilateral convulsion. 28% of PSS were generalized onset seizures [10]. In contrast to a study which documented that seizures were more often generalized than partial [11].

This study found that, the brain imaging of the cases group who developed seizures showed that, 50% of the cases have arterial ischemic infarction, 30% venous infarction, 6.67% ischemic infarction with haemorrhagic transformation, 6.67% intracerebral haemorrhage and 6.67% have subarachnoid haemorrhage. These results are consistent with a study which state that, the prevalence of seizures after ischemic stroke is higher than hemorrhagic stroke. The etiology of stroke due to infarction is significantly more prevalent than bleeding, so that the main incidence of seizures is related to the cerebral vascular occlusive disease [12]. In contrast to a study revealed a higher incidence of seizures in patients with hemorrhagic stroke than ischemic stroke [13]. Another study conducted in Indonesia, did not find a correlation between the incidence of early seizures and the type of stroke [14].

This study was in agreement with the study by Copenhagen stroke, they did not find a significant relationship between cortical involvement and early onset seizures [15]. In contrast to studies which state that the prevalence of seizures in cortical lesions is higher than in subcortical Lesions. Cortical involvement is a risk factor for the development of seizures in ischemic

Table 6 Difference in functional outcome during discharge of the patients in the three groups

| | Group | | | Fisher's Exact test | |
|--------------------------|----------|-------------|-------------|---------------------|-----|
| | Control | DCL | Fits | p value | Sig |
| | N (%) | N (%) | N (%) | | |
| Functional outcome | | | | | |
| Favorable (MRS < 3) | 18 (60%) | 10 (33.33%) | 16 (53.33%) | 0.115 | NS |
| Unfavourable (MRS > = 3) | 12 (40%) | 16 (53.33%) | 12 (40%) | | |
| Died | 0 (0%) | 4 (13.33%) | 2 (6.67%) | | |

mRS: modified Rankin scale; DCL: disturbed conscious level

stroke and hemorrhagic stroke [16]. Cortical irritation is thought to be the cause of the higher epileptogenicity of stroke.

The incidence of seizures was higher for the patients with PACS (33.33%), than TACS (13.33%), PCS (10%) and lacunar syndrome (0%). However, there was no statistically significant difference between the three groups. The same as study that observed that TACS was not significantly associated with an increased post-stroke seizure risk, probably because the area affected by stroke is too large for the surviving neurons to get excited or carry epileptiform activity from the area of gliosis [17]. Strokes in anterior vascular territories are more likely to cause seizures compared to posterior ones attributed to the fact that the anterior vascular territory involves larger areas of the cortex [16].

Most EEG findings in this study were focal slowing, focal epileptiform activities, generalized epileptiform activities and PLEDS. The same as the study found that, focal or diffuse slowing was found in 84% of them and lateralized periodic discharges, which are related to interictal epileptiform abnormalities, in 6% [18]. In addition, a study found that, diffuse slowing of background activity was the most common (67/232, 28.9%). Focal slowing and epileptiform activity were noted in 50/232 (21.5%) and 115/232 (49.6%), respectively. periodic lateralized epileptiform discharges (PLEDs) were found in 8 (7.0%) [19].

This study showed that there was no significant relationship between seizures and early treatment with Rtpa and thrombectomy. A study also, could not find association between treatment modality and occurrence of seizures [20]. However, systemic thrombolysis was a significant predictor of early seizures in two studies including a multicenter trial [21].

This study found that, there was no statistically significant difference between the three groups as regard the functional outcome. The same as a study found that the acute clinical epileptic seizure does not appear to be an independent predictor of the unfavorable outcome at hospital discharge [22]. In contrast to a study found that early seizures after stroke was associated with poorer functional outcome at hospital discharge [7].

The study had some limitations as the small sample size, which may limit the strength of the results. This is hospital—tertiary health care center-based study, limiting generalization of the findings of the study.

Conclusions

Upon studying the clinical characteristics of early onset seizures after stroke it was found that, focal to bilateral tonic clonic and focal aware seizures were the most prevalent type of early onset seizures. Most EEG findings

in this study were focal slowing, focal epileptiform activities, generalized epileptiform activities and PLEDS. Age, gender, diabetes mellitus, hypertension, heart diseases, collagen disease and carotid stenosis did not have significant association with early seizures. Early seizures did not seem to be associated with worse functional outcome at hospital discharge after acute stroke.

Abbreviations

CVS: Cerebrovascular stroke; PSS: Post-stroke seizures; EEG: Electroencephalogram; DCL: Disturbed conscious level; ILAE: International league against epilepsy; mRS: Modified Rankin Scale; PLEDS: Periodic lateralized epileptic discharges; OCSF: Oxfordshire community stroke project; PACS: Partial anterior circulation syndrome; TACS: Total anterior circulation syndrome; PCS: Posterior circulation syndrome.

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Author contributions

SH: data collection and research project execution. MF: contribution to the concept and design, drafting the manuscript. AA: conception of the work, manuscript revision. ED: acquisition of data and analysis of data, EH: analysis and interpretation of data. HA: conception of the work, Approved the version to be published. NE: conception and design, revised the manuscript critically for important intellectual content. All authors have agreed to conditions noted on the Authorship Agreement Form and have read and approved the final version submitted. The content of the manuscript has not been published, or submitted for publication elsewhere. All authors read and approved the final manuscript.

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Availability of data and materials

Data set is available as master sheet in Excel format and publicly available in Neurology department, Ain Shams University through communicating corresponding author.

Declarations

Ethics approval and consent to participate

The study protocol was approved by Ain Shams University, Faculty of Medicine Research Ethic Committee FWA 000017585 in 2020. Written informed consent was obtained from the patients participating in the study, or their first-degree relatives if the patient was unable to provide consent, after informing them about the study rationale and their right to withdraw from the study at any time without any consequences.

Consent for publication

Not applicable.

Competing interests

All authors declare that they have no conflict interest.

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