The Egyptian Journal of Hospital Medicine (April 2025) Vol. 99, Page 1558-1565

Clinical, Neuroimaging and Serum Heat Shock 70 kDa Protein-8 as Predictors of Post Stroke Epilepsy: A Prospective Cross-Sectional Study

Ahmed Hamed Ahmed Abo Mosalam[1], Azza ElMongui ElMongui[1], Shaimaa Rabea[2], Hossam Mohamed Egila[1]

1 Department of Neurology, 2 Department of Pathology, Faculty of Medicine, Mansoura University, Mansoura, Egypt

Corresponding author: Ahmed Hamed Ahmed Abo Mosalam, **Email:** bapr.mosalam@gmail.com, **Tel:** +20 10 95081006

ABSTRACT

Background: Heat Shock 70 kDa protein-8 (Hsc70) is a chaperone protein that is related to heat shock protein 70 family. It stabilizes or breaks down mutant proteins and helps misfolded and newly translated proteins fold correctly. It facilitates signal transmission, apoptosis, autophagy, protein homeostasis, cell proliferation, and differentiation.

Objective: This study aimed to compare blood biomarker Hsc70 with clinical and neuroimaging data to predict poststroke epilepsy (PSE).

Patients and methods: There were 15 control subjects and 80 patients. To assess onset of epilepsy in cases, ischemic stroke was identified in 65 individuals and hemorrhagic stroke in 15 patients. They were admitted to the Neurology Department, Mansoura University Hospital and Mansoura International Hospital during the period from May 2023 to May 2024. They were diagnosed clinically and confirmed radiologically. Serum Hsc70 protein was done to patients and control.

Results: Serum Hsc70 protein showed statistically significant downregulation between cases who developed epilepsy in comparison to cases who didn't develop epilepsy ($p = 0.046$). It had mean values of 2.06, 1.54, and 0.3 ng/ml in cases who did not develop epilepsy, cases who developed epilepsy and control groups, respectively. When a cut-off value < 2.32 ng/ml is applied, serum Hsc70 had sensitivity and specificity of 77.8% and 62.4%, respectively, for prediction of epilepsy after stroke. National Institutes of Health Stroke Scale (NIHSS) and Modified Ranking Scale (mRS) demonstrated a significant increase in patients who developed epilepsy ($p < 0.005$).

Conclusion: The statistically significant risk factors for developing PSE include stroke severity, degree of disability, temporal lobe stroke and downregulation of Hsc70.

Keywords: Serum heat shock 70 kDa protein-8, Epilepsy, Clinical and neuroimaging data.

INTRODUCTION

Acute brain insults such as head trauma, stroke, or infection of the central nervous system cause between 20% and 60% of epilepsies [1]. With an incidence of 2% to 20%, PSE accounts for around half of recently diagnosed epilepsies in those over age of 60 [2].

Seizures following a stroke that happen within seven days can be classified as early, and those that happen later can be classified as late [3]. According to a population-based study, the 10-year probability of recurrence is 71.5% higher for late-onset seizures (LOS). Therefore, International League Against Epilepsy (ILAE) standards classify cases with a single late seizure as having structural epilepsy [4].

Poststroke epilepsy is more likely in younger patients, those with hemorrhagic strokes, those with cortical involvement, and those with more severe strokes. In the days, weeks, months, or years that follow a stroke, the brain goes through an epileptogenic process that leaves it vulnerable to recurring, spontaneous seizures [5].

According to recent research, the mechanisms causing this condition might be comparable in a number of acute brain events (such as infections, strokes, and head trauma). To repair the brain damage caused by these assaults, a variety of inflammatory mediators are generated, including prostaglandins, complement, cytokines, chemokines, damage-associated molecular patterns (DAMPs), and transforming growth factor β (TGF-β). Chronic neuroinflammation causes neuron and astrocyte dysfunction, aberrant neurogenesis, hyperexcitability, neuronal death, gliosis, and synaptic transmission. Thus, epileptogenesis may involve all these phases. One of these inflammatory mediators is HSC 70 kDa protein-8, a chaperone protein and member of the HSC 70 family. It stabilizes or breaks down mutant proteins and helps newly translated and misfolded proteins fold correctly. Its functions participate in biologic processes such as signal transduction, apoptosis, autophagy, protein homeostasis, and cell growth and differentiation [1].

In order to detect post-stroke epilepsy, this study aimed to connect clinical and neuroimaging studies of stroke patients with the blood biomarker HSC 70 kDa protein-8.

PATIENTS AND METHODS

Study design

Eighty patients and fifteen controls participated in a planned cross-sectional study. To assess onset of epilepsy in cases, 65 individuals were diagnosed with ischaemic stroke and 15 with hemorrhagic stroke. At Mansoura University Hospital and Mansoura International Hospital, they were admitted to the Neurology Department. The patients were diagnosed clinically and confirmed radiologically during the period from May 2023 to May 2024.

Received: 04/11/2024
Accepted: 05/01/2025

Inclusion criteria: Individuals diagnosed with an ischaemic or hemorrhagic stroke who were older than 18 years were included.

Exclusion criteria: Cases with a history of epilepsy prior to stroke, transient ischaemic attack, subarachnoid haemorrhage, arteriovenous malformation, subdural haematoma, seizure-causing medical conditions, inadequate information in medical records, and patients with ischaemic stroke who received thrombolysis or thrombectomy.

Clinical assessment: Cases were subjected to complete neurological history and examination. It included personal history, NIHSS to determine severity of stroke, Montreal Cognitive Assessment (MoCA) to asses cognition, Barthel scale to assess performance in basic activity of daily living (ADL), mRS to assess degree of disability, Trial of ORG10172 in acute ischaemic stroke (AIS) classification (TOAST) to identify stroke etiology, Oxford Community Stroke Project Classification (OCSP) to predict the site and size of infarction.

Radiological assessment: CT brain by SOMATOMA sensation CT scanner or MRI brain by GE MAGNETOM 1.5T MRI machine were performed to all patients to assess site and type of stroke.

Laboratory assessment: Serum heat shock 70kDa protein-8 (ng/ml) was obtained from 80 patients and 15 control. At least 5 ml of blood were collected in serum sample tubes and centrifuged at 4000 rpm for fifteen min at 4 ºC and plasma aliquots were frozen at −20ºC until analysis. Serum heat shock 70kDa protein-8 cut-off value was > 0.715 ng/ml.

Ethical consideration and consent: Patients or their family members were asked to provide written informed permissions and were fully informed of the aim of the study and its entire process and were given the assurance that their medical care would not be impacted if they declined to take part. Any patient has the right to refuse to complete the interview at any time with no consequences. The research ethics committee of Mansoura University's medical faculty granted approval (MS.22.04.1964 on the 23rd of April 2022) and followed the Declaration of Helsinki.

Statistical analysis

The SPSS V.25 application for Microsoft Windows 10 and Microsoft Excel 2017 were used to tabulate and statistically analyze the results. We used two different statistical methods: ***Descriptive statistics****:* For parametric quantitative data, the data was described using the mean and SD, and for non-parametric quantitative data, the median (Range). For qualitative data, frequency and percentage were used. Multiplying total number of observations by their total number yields the mean.

Analytical statistics: that includes the tests: Chi-square test was utilized to compare two groups or more in terms of one qualitative variable, Standard student-t test (t) was used to compare two groups in terms of normally distributed (parametric) quantitative data, Fisher's exact test: was used instead when the expected frequency was less than 5 in 2x2 tables while Monte-Carlo test was used in > 2x2 tables and U test, which is a non-parametric test of Student's t-test. It is used to demonstrate if a non-normally distributed quantitative variable significantly differs between two groups. If you have non-parametric quantitative data and wanted to compare three groups, you can use the Kruskal Wallis test. ROC curve: It is calculated by plotting sensitivity (TP) versus 1-specificity (FP) at various cut-off values. The test's diagnostic efficacy is indicated by the area of the ROC curve. For statistical purposes, a P value ≤ 0.05 was deemed significant.

RESULTS

Eighty people were a part of this prospective case control study; 65 had an ischaemic stroke and 15 had hemorrhagic stroke. 15 were healthy controls who were matched for age and gender. Neither age nor gender significantly differed between the two groups (p = 0.837 and 0.593, respectively) (Table 1).

Table (1): Demographic data in the two studied groups

	Groups				Test of significance
	Cases group (N=80)		Control group (N=15)		
Age (50-80Years)	69.80 ± 6.67		70.20 ± 8.00		t = - 0.207 P = 0.837
Gender	N	%	N	%	X^2 = 0.286 P = 0.593
Males	42	52.5	9	60	
Females	38	47.5	6	40	

P: probability. χ2= Chi-square test t: Independent samples t-test

Five patients (6.25%) experienced seizures at an early stage, whereas eight patients (10%) suffered seizures at a later stage. Among the 5 cases of early-onset seizures (EOS), 2 later-onset seizures, and 7 late-onset seizures all resulted in the development of epilepsy. Early-onset seizures and late onset seizures showed statistically significant increase in the epilepsy group (P = 0.012 and P = 0.024 respectively). Statistical analysis revealed no difference between the two groups for the occurrence of medical comorbidities (p > 0.05) (Table 2).

Table (2): Risk factors in the cases group (N=80) according to development of epilepsy

Variables	Groups				Test of significance
	No epilepsy (N=71)		Epilepsy (N=9)		
Smoking	N	%	N	%	FET = 0.885 P = 0.347
	14	19.7 %	3	33.3 %	
HTN	45	63.4 %	6	66.7 %	$\chi 2$ = 0.037 P = 0.847
DM	24	33.8 %	3	33.3 %	FET = 0.010 P = 0.978
Dyslipidaemia	41	57.7 %	6	66.7 %	$\chi 2$ = 0.262 P = 0.609
Statin use	40	56.3 %	5	55.6 %	$\chi 2$ = 0.016 P = 0.964
AF	27	46.6 %	3	42.9 %	FET = 0.075 P = 0.784
Early onset seizures	3	4.2 %	2	22.2 %	$\chi 2$ = 6.354 P = 0.012*
Late onset seizures	1	1.4%	7	77.8%	*FET = 5.099* *P = 0.024**

P: probability, $\chi 2$= Chi-square test, FET= Fischer's exact test, *: Statistically significant (P < 0.05)

Regarding the site of stroke, there was a statistically significant increase in temporal lobe location (P = 0.047). Type of stroke did not reveal significant difference between the two groups, (p > 0.777). The incidence of haemorrhagic transformation in ischemic cases was 10.3% and 14.3% in the two groups respectively (Table 3).

Table (3): Stroke criteria in the cases groups

Variables	Groups				Test of significance
	No epilepsy (N=71)		Epilepsy (N=9)		
Stroke type	N	%	N	%	FET= 0.080 P= 0.777
Ischemic	58	81.7	7	77.8	
Haemorrhagic	13	18.3	2	22.2	
	(N=58)		(N=7)		
Symptomatic haemorrhagic transformation	6	10.3	1	14.3	FET= 0.101 P= 0.751
Site of stroke					
Frontal lobe	12	16.9	2	22.2	FET = 0.215 P = 0.756
Parietal lobe	30	42.3	3	33.3	FET = 1.456 P = 0.124
Temporal lobe	19	26.8	4	44.4	FET = 3.002 P = 0.047*
Occipital lobe	10	14.1	0	0	FET = 2.246 P = 0.082

P: probability. FET= Fischer's exact test, *: Statistically significant (P < 0.05)

Basal NIHSS and NIHSS at discharge showed a statistically significant increase in patients who developed epilepsy. On the other hand, Barthel scales showed a statistically significant decline in epilepsy cases. While, mRS revealed a statistically highly significant increase in patients who developed epilepsy, MoCA revealed a statistically highly significant decline in epilepsy cases (Table 4).

Table (4): Analysis of NIHSS, Montreal Cognitive Assessment (MoCA), Barthel scale for daily activities and mRS in the cases' groups

	Groups		Test of significance
	No epilepsy (N=71)	Epilepsy (N=9)	
Basal NIHSS	15 (3 – 28)	25 (12 – 34)	z = - 2.850 P = 0.004*
MoCA	23 (18 – 28)	17 (13 – 22)	z = - 3.922 P < 0.001**
Barthel scale	70 (50 – 90)	50 (35 – 65)	z = - 3.449 P = 0.001*
mRS	2 (1 – 4)	4 (3 – 5)	z = - 4.008 P < 0.001**
NIHSS at discharge	12 (2 - 25)	20 (10 – 28)	z = - 2.821 P = 0.005*

P: probability. z: Mann-Whitney U-test, *: Statistically significant (P < 0.05) **: Statistically highly significant (P < 0.001)

Regarding TOAST classification of the ischemic stroke cases (N=65), cardio embolism was the most common cause in both groups. When, it came to such classification, there was no statistically significant difference between the two groups (p = 0.241) (Table 5).

Table (5): TOAST classification in the cases groups (Cases with ischemic stroke only)

TOAST	Groups				Test of significance
	No epilepsy (N=58)		Epilepsy (N=7)		
Cardio embolism	**N**	**%**	**N**	**%**	MC = 5.491 P= 0.241
	27	46.6	3	42.9	
Large artery Atherosclerosis	25	43.1	2	28.6	
Small artery occlusion	3	5.2	0	0	
Other determined	2	3.4	1	14.3	
Undetermined	1	1.7	1	14.3	

P: probability. MC= Montecarlo test *: Statistically significant (P < 0.05)

OCSP classification did not show significant differences between ischemic stroke cases who developed and did not develop epilepsy (p = 0.802). LACI (lacunar infarct) and partial anterior circulation infarct (PACI) attributed for most cases in both groups. Other subtypes included total anterior circulation infarcts (TACI) and posterior circulation infarct (POCI) **(Table 6).**

Table (6): OCSP classification in the cases groups (Cases with ischemic stroke only)

OCSP	Groups				Test of significance
	No epilepsy (N=58)		Epilepsy (N=7)		
Lacunar infarct	**N**	**%**	**N**	**%**	MC = 0.996 P= 0.802
	20	34.5	2	28.6	
Partial anterior circulation infarct	23	39.7	2	28.6	
Total anterior circulation infarct	11	19	2	28.6	
Posterior circulation infarct	4	6.9	1	14.3	

P: probability. MC= Montecarlo test *: Statistically significant (P < 0.05)

Serum HSC70 showed statistically significant downregulation in patients who developed epilepsy compared to those who did not develop epilepsy (p1 = 0.046**).** Serum HSC70 showed statistically highly significant downregulation in control compared to cases (p2< 0.001**)** (Table 7).

Table (7): Analysis of Hsc70 level in the study groups

Hsc70 level	Groups			Test of significance	
	No epilepsy (N=71)	Epilepsy (N=9)	Control (N=15)		
Mean ± SD	2.06 ± 0.68	1.54 ± 0.76	0.30 ± 0.18	KW = 39.902 P < 0.001**	P1= 0.046* P2 < 0.001** P2 < 0.001**
Range	2.02 (0.86 – 3.83)	1.37 (0.55 – 2.79)	0.26 (0.04 - 0.59)		

P: probability. KW= Kruskal Wallis test *: Statistically significant (P < 0.05)
**: Statistically highly significant (P < 0.001) P1: Significance between non epileptic and epileptic.
P2: Significance between non epileptic and control, P2: Significance between epileptic and control.

To differentiate cases from control we had a cut-off value > 0.715 ng/ml, HSC70 with sensitivity and specificity of 95.4% and 92.6% respectively and an accuracy of 93.6%. Serum HSC70 showed statistically highly significant downregulation in control compared to cases (p < *0.001*) (Table 8). Normally present in unstressed settings, Hsc70 is modestly activated under stress and plays a role in protein synthesis [6].

Table (8): Diagnostic value of Hsc70 level to differentiate cases (N=80) from control (N=15)

Diagnostic criteria	Hsc70 level
Area under the curve	0.953
Cut off point	> 0.715
Sensitivity	95.4 %
Specificity	92.6 %
Negative predictive value	92.3 %
Positive predictive value	94.2 %
Accuracy	93.6 %
P	< 0.001**

P: probability. *: significant p value (< 0.05). **: Statistically highly significant (P < 0.001).

Serum Hsc70 had sensitivity and specificity of 77.8% and 62.4% respectively to predict poststroke epilepsy (when a cut-off value < 2.32 ng/ml is applied). Serum HSC70 showed statistically significant downregulation in patients who developed epilepsy compared to those who did not develop epilepsy (p = 0.042) (Table 9).

Table (9): Diagnostic value of Hsc70 level to differentiate cases with epilepsy from cases who did not develop epilepsy

Diagnostic criteria	Hsc70 level
Area under the curve	0.700
Cut off point	< 2.32
Sensitivity	77.8 %
Specificity	62.4 %
Negative predictive value	68.4 %
Positive predictive value	76.2 %
Accuracy	70.4 %
P	0.042*

P: probability, *: significant p value (< 0.05).

DISCUSSION

Eleven percent of epilepsy cases involve cerebrovascular illness, and the percentage rises with age, accounting for as much as 45% of incidence cases in the elderly (those over 65) [7]. The primary risk factor for post-stroke status epilepticus (PSSE), which typically manifests in the initial days following a stroke, is substantial cortical involvement (cortical infarction or lobar haemorrhage) [8].

The current study showed that post-stroke epilepsy occurred in 11.25% (nine cases) of all stroke cases (eighty cases). Seven of them (77.8%) had late-onset seizures (after one week), while the remaining two (22.2%) had early onset seizures (within one week of the stroke event). Our study is close to the study of **Sarfo *et al.*** [9] who found that 11.4% of 1100 stroke survivors in one Ghanaian Tertiary Medical Center experienced post-stroke epilepsy. The authors discovered that PSE was most prevalent in survivors of ischaemic stroke (12.1%), followed by survivors of intracerebral hemorrhagic stroke (10.3%), and survivors of sub-arachnoid haemorrhage (4.4%). Our research is similarly comparable to that conducted by **Brondani *et al.*** [14] who found that following thrombolysis for AIS treatment, 15 (9.8%) patients acquired epilepsy, and 21 (13.7%) patients experienced seizures. On the contrary, **Abraira *et al.*** [10] found that from cohort of 1115 stroke cases, 895 cases were included with a 4.8 years median follow up, where 5.7 % developed epilepsy. Out of 3310 patients who were followed up for a mean of 3.8 and median of 2.0 years without history of epilepsy presenting with first stroke (6.4%) developed PSE according to **Graham *et al.*** [11].

Our study showed that out of all 80 cases, 5 cases had early onset seizure, and 8 cases had late onset seizure. 40% of early onset seizure developed to epilepsy and 87.5 % of late onset seizures developed to epilepsy. Most EOS happened within the initial 48 hours, while most late-onset seizures occurred after six months, according to a one-year follow-up. **Redfors *et al.*** [12] observed that 7 (27%) of the 26 patients (2.4%) who experienced early seizures (ES) went on to develop post-stroke epilepsy (PSE). During follow-up, 84 patients (7.9 %) developed PSE and 7 cases (0.6 %) had status epilepticus. The authors found that most patients in their study developed PSE within four years after the index stroke. However, they discovered that a second stroke

preceded only roughly 50% of seizures that occurred more than four years following the index stroke. **Kulhari *et al.*** [13] showed that out of 8.6% of cases with ischaemic stroke who experienced seizures in the Seizure after Stroke Study (SSS), 56% of those seizures occurred at an early stage, and 44% occurred at a later stage. Most early onset seizures occurred during the first 24 hours [14]**.** Their median follow-up was 214 days.

Gliotic scarring, neurodegeneration, neurogenesis, apoptosis, altered synaptic plasticity, and selective neuronal loss are the reasons of late seizures following stroke, whereas disturbance of the blood-brain barrier, cellular hypoxia, electrolyte disturbance, and ion channel malfunction are the causes of early seizures [15].

After stroke, late-onset seizures are more likely to cause epilepsy. In a study by **Kulhari *et al.*** [13] **,** they noted in cases with ischaemic or hemorrhagic stroke, epilepsy developed in ≈30% of early onset cases and 90% of late onset cases. **Haapaniemi *et al.*** [16] found that the risk of epilepsy is higher in cases who developed an early onset seizure (30%) than in cases with stroke in general (5%–20%). A statistical link between hemorrhagic stroke and poststroke epilepsy was not possible due to the small number of hemorrhagic stroke cases in our research. **Doria *et al.*** [17] discovered that those who experience intracerebral haemorrhage are more likely to have epilepsy than those who had an ischaemic stroke (15% versus 9%). The authors discovered that the mechanical consequences of the growing haemorrhage and/or acute blood metabolism products, as well as persistent hemosiderin depositions and gliotic scarring, cause seizures in cases of intracerebral haemorrhage. Predictors of PSE include the following: Lesion size, haemorrhage, TACI, early onset seizures, stroke severity, cortical involvement, and young age after stroke [18]**.** Larger volumes and cortical placement significantly enhance the likelihood of seizures following a stroke [19].

According to our research, there was a significant rise in the number of stroke victims who acquired epilepsy in the temporal lobe (44%).

In the same line as our results**, Feyissa *et al.*** [20] noted that there has also been evidence of a high correlation between stroke-related epilepsy (STRE) and temporal lobe infarct. Also, in a meta-analysis by **Zhang *et al.*** [21]**.** Based on their analysis of 12 research (n = 6484), they found that certain brain areas, such as the parieto-temporal cortex, supramarginal gyrus, and superior temporal gyrus, were associated with an increased likelihood of STRE. Furthermore, **Weiss *et al.*** [22] noticed significant differences in the following areas between the STRE and control groups: parietal operculum, superior occipital gyrus, lingual gyrus, postcentral gyrus, supramarginal gyrus, angular gyrus, transverse temporal gyri, and superior temporal gyrus.

According to our research, patients who acquired epilepsy had statistically significant increases in both basal and discharge NIHSS. Basal NIHSS had median values of 15 and 25, while discharge NIHSS had median values of 12 and 20 in the group who did not develop epilepsy and epilepsy group, respectively (P = 0.004). Patients who had epilepsy increased statistically significantly, according to the Modified Ranking Scale. The group without epilepsy had median values of 2, and the group with epilepsy had median values of 3 (P < 0.001). In agreement with our study **van Tuijl *et al.*** [23] found statistically significantly higher NIHSS at the time of their research in cases with PSE (mean NIHSS 4.9 vs 1.6 in patients with stroke only, $p < 0.01$). When comparing patients with PSE to those with stroke alone, the investigators discovered that the mRS was statistically considerably greater in the former group. More impairment in PSE patients is indicated by a higher mRS [24]. **Abdel Ghani *et al.*** [25] compared the case group (acute ischaemic stroke with early seizures) to control group (acute ischaemic stroke without seizures), the difference in mean NIHSS score was statistically significant (P < 0.001). Also, this is in agreement with **Tanaka *et al.*** [26] who found that the NIHSS score is associated with the degree of early neurological impairment and disability following a stroke. In contrast, **Castro-Apolo *et al.*** [27] discovered that PSS patients had a higher NIHSS (median=9) than the healthy controls (median=6.5), but it did not prove to be a statistically significant predictor of PSS (p=0.21). The authors enrolled 42 patients with new-onset seizures owing to AIS and 60 healthy controls who underwent ischaemic stroke including the cortex without developing seizures. Furthermore, our results are in agreement with **Arntz *et al.*** [28] who suggested that the functional outcome as judged by the mRS was worse for patients whose first seizure occurred after their first ischaemic stroke. Brain tissue in an ischaemic state already lacks sufficient oxygen and energy supply, and seizures can make that situation worse, leading to a larger infarct and slower motor recovery. Similarly, **Agarwal *et al.*** [29]**,** showed that early seizure patients had a significantly worse functional result 3 months following their stroke.

This study showed that regarding the TOAST classification, cardio embolism was the most common cause in epileptic and non-epileptic groups (46.6% and 42.9% respectively), followed by large artery atherosclerosis (43.1% and 28.6% respectively). Other causes included small artery occlusion, other determined causes, and undetermined causes. In addition, insignificant difference was noted between both groups regarding that classification.

Benbir *et al.* [30] discovered that in terms of TOAST criteria, there was insignificant difference between subjects with and without post-ischemic epilepsy. They found that among the subgroups of ischaemic stroke, 36.2% of the epileptic group and 35.7% of the non-epileptic group had atherothrombotic post-stroke epilepsy, 27.8% of the epileptic group and 28% of the non-epileptic group had cardioembolic post-stroke epilepsy, and 11.1% of the epileptic group and

21.5% of the non-epileptic group had PSE after lacunar infarctions. The assessment of the correlation between the presence of PSE and the localization of the ischaemic strokes displayed that the commonest arterial territory was middle cerebral artery (63.9%, 23 cases).

There was no statistically significant difference in OCSP classification between ischaemic stroke patients who developed epilepsy and those who did not, according to the current study. LACI and PACI attributed for most cases. Two more subtypes are POCI and TACI. Our study may have a significant impact on OCSP classification due to the small number of instances. The OCSP classification has been displayed to predict size and cortical location**.** In previous studies by **Ferlazzo *et al.*** [18] , they revealed that TACI and PACI were independently accompanied by PSE**.** Furthermore**, Borges *et al.*** [31] reported that based on the OCSP classification, 40% TACS, 37% PACS, 10% LACS, and 13% POCS.

The release of HSC70 occurs during the neuroinflammation phase following a stroke; it is a member of the DAMPs protein family [1]. Individuals onset epilepsy were also associated with a reduction in Hsc70 protein. Normally present in unstressed settings, Hsc70 is modestly activated under stress and plays a role in protein synthesis [6]**.**

The present investigation demonstrated that serum Hsc70 protein was significantly downregulated in individuals with epilepsy compared to non-epilepsy patients (p=0.046). The control group, patients with no epilepsy, and those with epilepsy had mean levels of 0.3 ng/ml, 1.54 ng/ml, and 2.06 ng/ml respectively. The levels of serum HSC70 were significantly decreased in the control group in comparison with the patients ($p < 0.001$).

ROC curve analysis of our study showed that serum Hsc70 had sensitivity and specificity of 77.8% and 62.4%, respectively, to predict poststroke epilepsy (when a cut-off value < 2.32 ng.ml is applied). In a prospective study by **Abraira *et al.*** [10] of 14 serological blood indicators in 1115 stroke cases they revealed that the HSC70 was significantly diminished in the epileptic group, and the low level of HSC70 is a biomarker that could be utilized in the prediction and determination of PSE. ROC curve analysis displayed that the optimum cutoff value of the seizure risk was 2.49. Hsc70 has neuroprotective actions, which act as molecular chaperones, encouraging the correct folding of proteins to keep protein homeostasis. The blood-brain barrier's integrity is compromised by lowering Hsc70, which changes the risk of PSE [32]**.**

CONCLUSION

Our research demonstrated that patients who acquired poststroke epilepsy had statistically significant increases in stroke severity and impairment level. The ischaemic stroke cases that developed epilepsy and those who did not did not significantly differ in terms of TOAST or OCSP categorisation. Together with clinical risk factors for predicting epilepsy after stroke, this study also discovered that statistically significant downregulation of Hsc70 was linked to the onset of poststroke epilepsy. Finding these alterations could be useful.

LIMITATIONS

Due to the small number of patients, one of our limitations was the possibility of negative effects. There was also only one-year follow-up. We did not include cortical affection, stroke size, or their correlation with epilepsy following a stroke. Treatment's effect on the development of PSE was not considered.

RECOMMENDATION

Future studies are encouraged to use larger study groups to validate, build upon, and test the hypothesis with greater power. Additional study is needed to validate this biomarker and gather blood samples at different times in order to better understand the dynamics of blood biomarkers.

Competing interests: a conflict of interest does not exist.

Funding: For the research, writing, and publication of this paper, the author did not receive any funding.

REFERENCE

1. **Klein P, Dingledine R, Aronica E *et al.* (2018):** Commonalities in epileptogenic processes from different acute brain insults: Do they translate? Epilepsia, 59 (1): 37-66.
2. **Feyissa A, Hasan T, Meschia J (2018):** Stroke-related epilepsy. European Journal of Neurology, 26 (1): 18.
3. **Beghi E, Carpio A, Forsgren L *et al.* (2010):** Recommendation for a definition of acute symptomatic seizure. Epilepsia, 51 (4): 671-5.
4. **Fisher R, Acevedo C, Arzimanoglou A *et al.* (2014):** ILAE Official Report: A practical clinical definition of epilepsy. Epilepsia, 55 (4): 475-82.
5. **Zelano J (2016):** Poststroke epilepsy: update and future directions. Ther Adv Neurol Disord, 9 (5): 424-35.
6. **Yang T, Hsu C, Liao W *et al.* (2008):** Heat shock protein 70 expression in epilepsy suggests stress rather than protection. Acta neuropathologica, 115: 219-30.
7. **Brigo F, Tezzon F, Nardone R (2014):** Late-onset seizures and risk of subsequent stroke: a systematic review. Epilepsy & Behavior, 31: 9-12.
8. **Moalla K, Damak M, Chakroun O *et al.* (2019):** Incidence and predictors of post-stroke epilepsy. Journal of the Neurological Sciences, 405: 114.
9. **Sarfo F, Akassi J, Obese V *et al.* (2020):** Prevalence and predictors of post-stroke epilepsy among Ghanaian stroke survivors. Journal of the Neurological Sciences, 418: 117138.
10. **Abraira L, Santamarina E, Cazorla S *et al.* (2020):** Blood biomarkers predictive of epilepsy after an acute stroke event. Epilepsia, 61 (10): 2244-53.
11. **Graham N, Crichton S, Koutroumanidis M *et al.* (2013):** Incidence and associations of poststroke epilepsy: the prospective South London Stroke Register. Stroke, 44 (3): 605-11.

12. **Redfors P, Holmegaard L, Pedersen A *et al.* (2020):** Long-term follow-up of post-stroke epilepsy after ischemic stroke: Room for improved epilepsy treatment. Seizure, 76: 50-5.
13. **Kulhari A, Strbian D, Sundararajan S (2014):** Early onset seizures in stroke. Stroke, 45 (12): e249-e51.
14. **Abraira L, Toledo M, Guzmán L *et al.* (2019):** Long-term epilepsy after early post-stroke status epilepticus. Seizure, 69: 193-7.
15. **Tanaka T, Ihara M, Fukuma K *et al.* (2024):** Pathophysiology, diagnosis, prognosis, and prevention of poststroke epilepsy: clinical and research implications. Neurology, 102 (11): e209450.
16. **Haapaniemi E, Strbian D, Rossi C *et al.* (2014):** The CAVE score for predicting late seizures after intracerebral hemorrhage. Stroke, 45 (7): 1971-6.
17. **Doria J, Forgacs P (2019):** Incidence, implications, and management of seizures following ischemic and hemorrhagic stroke. Current neurology and neuroscience reports, 19: 1-8.
18. **Ferlazzo E, Gasparini S, Beghi E *et al.* (2016):** Epilepsy in cerebrovascular diseases: review of experimental and clinical data with meta-analysis of risk factors. Epilepsia, 57 (8): 1205-14.
19. **Alvarez V (2014):**Acute seizures in the acute ischemic stroke setting: a step forward in their description. Lippincott Williams & Wilkins Hagerstown, Vol. 82, Pp: 740-741.
20. **Feyissa A, Hasan T, Meschia J (2019):** Stroke-related epilepsy. European journal of neurology, 26 (1): 18-e3.
21. **Zhang C, Wang X, Wang Y *et al.* (2014):** Risk factors for post-stroke seizures: a systematic review and meta-analysis. Epilepsy research, 108 (10): 1806-16.
22. **Weiss V, Říha P, Doležalová I *et al.* (2023):** Brain Areas Predisposing to the Stroke-Related Epilepsy Development. Acta Neurologica Scandinavica, 1: 1439121.
23. **Van Tuijl J, Van Raak E, Van Oostenbrugge R *et al.* (2020):** Cognition and quality of life in patients with poststroke epilepsy: A case–control study. Epilepsy & Behavior, 104: 106444.
24. **Arntz R, Maaijwee N, Rutten-Jacobs L *et al.* (2013):** Epilepsy after TIA or stroke in young patients impairs long-term functional outcome: the FUTURE Study. Neurology, 81 (22): 1907-13.
25. **Abdel Ghani A, Gouda T, Al Basheir H *et al.* (2022):** Predictors and Outcome of Early Post Stroke Seizures. The Egyptian Journal of Hospital Medicine, 89 (2): 6197-61200.
26. **Tanaka T, Yamagami H, Ihara M *et al.* (2015):** Seizure outcomes and predictors of recurrent post-stroke seizure: a retrospective observational cohort study. PLoS One, 10 (8): e0136200.
27. **Castro-Apolo R, Huang J, Vinan-Vega M *et al.* (2018):** Outcome and predictive factors in post-stroke seizures: a retrospective case-control study. Seizure, 62: 11-6.
28. **Arntz R, Maaijwee N, Rutten-Jacobs L *et al.* (2013):** Epilepsy after TIA or stroke in young patients impairs long-term functional outcome. Neurology, 81 (22): 1907-13.
29. **Agarwal A, Sharma J, Srivastava M *et al.* (2021):** Early post-stroke seizures in acute ischemic stroke: a prospective cohort study. Annals of Indian Academy of Neurology, 24 (4): 580-5.
30. **Benbir G, Ince B, Bozluolcay M (2006):** The epıdemıology of post-stroke epılepsy accordıng to stroke subtypes. Acta neurologica scandinavica, 114 (1): 8-12.
31. **Borges D, Silva M, Ferreira A *et al.* (2018):** Clinical usefulness of the electroencephalogram in acute stroke: a preliminary study. Archives in Neurology & Neuroscience, 1(3): 1-7.
32. **Liang M, Zhang L, Geng Z (2021):** Advances in the Development of Biomarkers for Poststroke Epilepsy. Biomed Res Int., 2021:5567046-.