A Prospective and Retrospective Analysis of Patients with Post-Stroke Epilepsy Presenting at Tertiary Care Hospital

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Abstract: Stroke is one of the most common causes of disability in Saudi Arabia and when seizures complicate the stroke, the disability, cost, psychological impact and post traumatic stress on the family are tremendously increased. As for the best of author's knowledge there is no available data regarding the incidence, frequency, outcome and the risk factors or predictors of seizures after stroke in Saudi Population. Our study was conducted in King Fahd Hospital located in Eastern Province of Saudi Arabia. It is the main tertiary care Hospital in the region. We collected our sample in three consecutive years from 2007 to 2009. In the first two years data was collected from medical records system and in the third year the data of patients and controls was collected from newly admitted stroke patients. The study concluded mean incidence of post stroke epilepsy (PSE) to be about 9.6 %. A lower blood sugar and higher Rankin Disability scores were found to be significantly higher amongst patients with post-stroke epilepsy. There was no significant difference in co morbid diseases on developing PSE. The present study also showed that the occurrence of post stroke epilepsy was positively associated with increasing age and male gender.

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1. Introduction:

Post stroke Epilepsy (PSE) is one of the major causes of epilepsy in elderly population (1,2). In most studies the percentage of seizures that starts after the age of 60 years is attributed to stroke (3). The frequency of post stroke epilepsy in various populations is reported between 2.3 % to 43 %. This high variability in frequency of epilepsy is suggested to be due to different ethnic groups of studies or the definition of post stroke epilepsy or methodology and study design (4,5). In our study post stroke epilepsy was defined as a single or multiple convulsive episode/s (Fit/s) after stroke and thought to be related to cerebral damage due to stroke regardless the time of onset following the stroke.

2. Materials and Methods:

Aim of the study:

To identify, gather and study the overall risk of (post stroke epilepsy) PSE and to find the predictors for PSE both retrospectively and prospectively.

Study:

The study included all patients admitted in the hospital with stroke over a period of one year prospectively and two years retrospectively , to determine the incidence , frequency, outcome and risk factors for seizures after stroke at the King Fahd Hospital, Hofuf (KFHH).

Stroke was defined according to WHO criteria and did not include patients with subarachnoid haemorrhage, rupture of AV malformation, transient ischemic attacks.

The seizures and epilepsy were defined according to the criteria defined by International League Against Epilepsy. PSE was defined as two or more attacks of seizures after stroke.

All patients had CT scan or MRI of the brain for the diagnosis and localization of stroke. The disability after stroke was measured by Rankin Score.

Data analysis and data processing:

Data were entered and processed using SPSS (Statistical Package for Social Science) version 16.0 (SPSS Inc. Chicago IL). Both descriptive and inferential statistics were applied as appropriate. Statistical tests of significance including t-test and Mann Whiteny tests for continuous variables, Chi-square, Fisher Exact and *Z* tests for proportions were used for categorical data to detect difference between groups. Spearman Correlation coefficient was used to generate the inter-relation matrix between variables. Multivariate logistic regression model was generated

to define the association between patients characteristic and Rankin Scores (independent) to the occurrence of post stroke epilepsy (dependent), Odds ratio, 95% Confidence intervals and P value were reported for model. P value of < 0.05 was applied as a level of significance.

3. Results:

A total of 492 patients with stroke were admitted in the three years period from 2007 to 2009.

Table 1 shows the percentage of post stroke epilepsy among admitted stroke patients the three tears period the incidence of PSE ranged from 10.1 to 10.6% with an overall average of 10.4%. The incidence of PSE did not show significant relation in relation to time.

Table 2 displays basic demographic and clinical characteristics of stroke patients in relation to the occurrence of PSE. Those with post stroke epilepsy were significantly older in age and predominantly females and of rural residence. With the exception of significantly higher proportions of myocardial, coronary heart disease and reported dyslipidemia, there was no significant difference regarding the frequency and nature of the encountered co-chronic morbidities between in relation to the occurrence of PSE, although hypertension was recorded in 81.6% among those with epileptic activity compared to 70% among those without the activity.

Table 3 demonstrates the clinical characteristics of patients included in relation to the presence of PSE. It reveals that the occurrence of epileptic activity was not related to the type of stroke encountered or blood pressure measurements at admission. On the other hand, those with post stroke epilepsy recorded a significantly lower random blood sugar levels at admission and deterioration of Rankin scores on admission. The most commonly encountered type of seizures were the secondary generalized Tonic Clonic Seizures (66.7) followed by status epilepticus and simple partial types. In 78.4% of patients with PSE, seizures were controlled by using a single antiepileptic drug. Recurrence of seizures was recorded in 43.1 % of cases with mortality rate of 7.8%.

Table 4 depicts the intercorrelation matrix of potential independent variables associated with the development of post stroke epilepsy. It shows that the occurrence of post stroke epilepsy was positively associated with increasing age of the patients and female gender and negatively correlated with random blood sugar level at admission. Higher Rankin Scores were significantly positively correlated with the development of post stroke epilepsy. Neither the nature of current or previous stroke nor the multiplicity of the co-morbid disease conditions were not significantly correlated with the development of epileptic activities in the included patients.

Table 5 demonstrates the multivariate logistic regression model of predictors for the development of post stroke epilepsy. Female gender, higher Rankin score at admission and lower random blood sugar levels were significant positive predictors for the development of post stroke epilepsy among the included patients.

4. Discussion:

In our study the percentage of post stroke epilepsy among all admitted stroke patients in three consecutive years averaged 9.6 % which is almost similar in frequency as reported in western literature (6, 7, 8). A slightly higher frequency is reported from India while lower frequency of PSE has been reported from China. The variation in the frequency of PSE is most likely due to enrolment of patients in the studies and the criteria of PSE adopted by various studies. It is to be noted though that the definition of PSE influences the frequency.

Authors who included all seizures after a stroke and/or all seizures after stroke without distinguishing between acute, early, and late seizures reported a higher frequency of PSE.

Stroke incidence increases with advancing age (9). Cerebrovascular disease is the number one cause of epilepsy in the elderly population.(10) In a study of unselected population of over 2 million people in England and Wales, Wallace and colleagues found that both age specific incidence and prevalence of epilepsy are higher in older people(11). Our study also found that occurrence of post stroke epilepsy was positively associated with increasing age of the patients. This finding was not different from some studies which did not find age to be a significant predictor for PSE(6) or others in which young age to be a weak predicting factor, but the relative risk of seizures in younger patients compared with older ones did not reach statistical significance(8). The studies are at variance with regard to preponderance of PSE with regard to gender. In our study, the female were significantly at higher risk to develop post stroke epilepsy while some other studies found more common among the male gender is at higher risk (9)

Our study did not find any significant correlation regarding ischemic versus hemorrhagic stroke for onset of PSE. Some other studies has shown higher frequency of PSE among hemorrhagic stroke compared to ischemic stroke (9 -12).

Although we did not compare the size of stroke lesion in relation the occurrence of PSE, however, we found strong correlation between Rankin score and onset of PSE. Some other studies have also

found correlation between the severity of stroke and PSE. (13)

Another important finding was that PSE patients have lower random blood sugar levels compared to those without seizures. We know that hypoglycaemia can induce seizures, however, in our study none of the patient presented with hypoglycaemia. One possibility is that patients with stroke and relatively lower blood sugar compared to normals may contribute to initiation of seizures. Further studies are needed to probe this observation. We did not find any other study showing this disparity. However, we did not find any correlation between other co morbidities and onset of PSE.

In conclusion, our study shows that frequency of PSE is relatively higher compared to other studies, and that age and severity of stroke are major risk factor for developing post stroke epilepsy.

Table1. Incidence of post stroke epilepsy from 2007 to 2009 among patients admitted to King Fahd Hospital-Al Hofuf.

Year	All cases of stroke		Stroke with epileptic activity		
	No.	%	No.	%	% out of total stroke (incidence)
2007	198	40.2	20	39.2	10.1
2008	151	30.7	16	31.4	10.6
2009	143	29.1	15	29.4	10.5
Total	492	100.0	51	100.0	10.4

Chi square for trend=1.34, P= 0.368

Table 2. Basic demographic and clinical characteristics of the included stroke patients.

Variables	**Cerebral stroke (N=492)**		**P value**
	With epilepsy (N=51) No. (%)	**Without epilepsy (N=441) No. (%)**	
- Gender:			
Males	20(39.2)	387(85.7)	
Females	31(60.8)	54(14.3)	0.0001[a]
- Residence:			
Urban	25(49.0)	290(65.8)	
Rural	22(43.1)	98(22.2)	0.004[a]
Bedouins	4(7.8)	53(12.0)	
- Age in years (mean ±SD)	64.0±17.5	54.8±11.3	0.004[b]
- Occupational status:			
Working	30(58.8)	292(66.2)	
None (retired/no job/housewives)	21(41.2)	149(33.7)	0.293[c]
- Co-morbid conditions: total	49(96.1)	429(97.3)	0.647[d]
Hypertension	11(21.6)	84(19.6)	0.806 [d]
Diabetes mellitus	2(3.9)	-	--
Diabètes mellitus + Hypertension	27(52.9)	178(41.5)	0.115 [d]
Diabetes+ hypertension+ CHD	2(3.9)	52(12.1)	0.142 [d]
Others!	5(9.8)	127(29.6)	0.006 [d]
Sickle cell disease	2(3.9)	-	--
None	2(3.9)	12(2.7)	0.965 [d]
- Previous Stroke: total	51(100.0)	441(100.0)	
Hemorrhagic	3(5.9)	32(7.3)	0.941 [d]
Ischemic	45(88.2)	383(68.4)	0.952 [d]
Both hemorrhagic/ischemic	2(3.9)	-	--
Transient ischemic attack (TIA)	1(2.0)	26(5.9)	0.398 [d]

! Includes: dyslipidemia, myocardial infraction, and coronary heart disease.

[a]: = Chi-square Fisher exact [b]= t-test, [c]= Chi-square [d] = *Z* test for proportions.

Table 3. Characteristics of the included patients in relation to the presence of epilepsy and current stroke.

Variables	Cerebral stroke (N=492) With epilepsy (N=51) No. (%)	Cerebral stroke (N=492) Without epilepsy (N=441) No. (%)	P value
- Current stroke type:			
Ischemic	34(66.7)	281(63.7)	
Hemorrhagic	17(33.3)	160(36.6)	0.677[a]
- Blood pressure on admission (mmHg):			
Systolic Mean ±SD	152.1±38.2	149.4±33.7	0.723[b]
Diastolic Mean ±SD	90.2±21.6	94.6±22.4	0.364[b]
- Random blood sugar level (mg/dl):			
Mean ±SD	115.5±60.9	180.7±117.3	0.008[b]
- **Rankin Scores:** median (mean ±SD)			
Baseline	3.5(3.46±1.34)	2.0(2.10±0.93)	0.001[c]
Admission	4.0(3.73±1.26)	2.0(2.15±0.94)	0.001[c]
Discharge	4.0(3.80±1.93)	2.0(1.54±1.07)	0.001[c]
- Type of seizures:			
Simple partial	5(9.8)	-	
Complex partial	2(3.9)	-	
Secondary generalized	3(5.9)	-	
Generalized GTC	34(66.7)	-	
Status epilepiticus	6(11.8)	-	
Undefined	1(2.0)	-	
- Seizure control:			
One antiepileptic drug	40(78.4)	-	
Two anti-epileptics	10(19.6)	-	
More than two drugs	1(2.0)	-	
- **Total Rankin score**: Median (mean ±SD)	3.75(3.78±1.77)	-	
- Recurrence of seizures:	22(43.1)	-	
- Mortality:	4(7.8)	-	

SD = Standard deviation. [a]: Fisher exact, [b]= t-test, [c]= Mann Whiteny test.

Table 4. Intercorrelation matrix of variables associated with epileptic seizures among the included cases of stroke.

Variables	2	3	4	5	6	7	8	9	10
1-Age	.236*	.054	-.114	.010	.146	.293**	.212*	.186	.330**
2- Gender		.093	-.258*	-.169	.122	.495**	.141	.183	.097
3-Co-morbidity			-.071	-.226*	-.080	.043	-.027	-.101	-.166
4-Random blood sugar				-.185	.020	-.348**	-.267*	-.365**	.579**
5-Previous stroke type					-.283	-.083	.072	.078	.124
6-Current stroke type						.294	-.283	.232	.239
7-Post stroke epilepsy							.488**	.576**	.579**
8-Rankin base line								.858**	.757**
9-Rankin admission									.831**
10-Rankin discharge									

Spearman's significant correlation at * P< 0.05, ** P < 0.001

Gender (1=male, 2=female), co-morbidity (1= multiple, 2= single), previous/current stroke type (Ischemic = 1, other =2), post-stroke epilepsy (0= none, 1= present).

Table 5. Multivariate logistic regression analysis of predictors for post stroke epilepsy.

Independent variables	*B* coefficient (SE)	Odds ratio (95% confidence intervals)	P value
- Gender	.883(.642)	3.18(1.76-5.71)	0.001
- Age	-.034(.037)	0.97(0.90-1.04)	0.358
- Random blood sugar level	-.236(.652)	1.81(1.09-3.03)	0.037
- Rankin scores on admission	.670(.891)	2.43(1.22-4.73)	0.041
- Rankin scores baseline	-.236(.652)	0.79(0.22-2.83)	0.305
Constant	-4.294		
χ^2 for the model	63.241		
P value for the model	0.001		
percent predicted	90.9		

SE= standard error. Gender (1=male, 2=female).

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