



Post Stroke Epilepsy, The Frequency, Predictive Factors and Prevalence in Sudanese Patients, A Prospective Multicentre Study Khartoum, Sudan 2018

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Abstract

Background: Post-stroke seizure and post-stroke epilepsy are common causes of hospital admissions, either as a presenting feature or as a complication after a stroke. They require appropriate management and support in long term.

Objective: To measure the frequency, predictive factors and prevalence of post stroke epilepsy among adults in Khartoum state, Sudan, 2018.

Methods: A prospective multicentre study conducted at four teaching hospitals located in Khartoum state as following; the National Centre for Neurological Science, Omdurman teaching hospital, Khartoum North Teaching Hospital and National Ribat Teaching Hospital. This study covered 140 study participants recruited from the study area within one year duration. Who have seizure with or after stroke came to hospital as a first presentation or for follow up, Data collected through structural closed ended questionnaire and checklist. Data entered, cleaned, analyzed using SPSS version 25.0.

Results: There is almost equal gender ratio male: female 1:1, 69.3% of them were above 60 years of age, 30 (46.9%) were males and 34 (53.1%) were females. Out of 64 patients with post stroke epilepsy, 41 (64.1%) were more than 60 years, 17 (26.6%) were 30 to 60 years and 6 (9.4%) of them were 16 to 30 years. Regarding risk factors, 42 (65.6%) had hypertension, 35 (54.7%) diabetes, 3 (4.7%) were smoker, 4 (6.3%) hypercholesterolemia, 6 (9.4%) had CHD and 5 (7.8%) had Atrial fibrillation. The most frequent types of seizures were generalized tonic clonic 54.7%, simple partial 10.9% then focal with secondary generalization 17.2%, 95.4% of them had power less than G4. Brain MRI & MRA Showed parietal lobe affection in 37.5%, frontal lobe in 12.5% and multiple lobar affection was found in 17.5%. Only 1.4% had poly spikes waves in EEG, 21.5% had atrial fibrillation in ECG, 26.4% had cardiac thrombus, 9.3% had valve disease in Echocardiography, and 20.7% had blood glucose more than 200 mg/dl. high potassium was found in 3.6%, low sodium in 2.9%, low calcium in 5%, low magnesium 3.6%, high urea in 16.4% and high creatinine in 15%. 20% of the study participants had intracranial hemorrhage, 80% had ischemic stroke. There is a significant association between them (p value =0.0029), it is noticed that being diagnosed as hemorrhagic stroke considered as main predictive factors for the future occurrence of Post stroke seizures. The prevalence of post stroke seizures among the study participants was 45.7%.

Conclusion: The study found that there is a significant association between post stroke seizures and hemorrhagic stroke (p value =0.0029). Hemorrhagic stroke considered as a main predictive factors for the future occurrence of Post stroke seizures. Hypertension followed by Diabetes was the main risk factors followed by cardiac thrombus and atrial fibrillation. Generalized seizures were common. The parietal lobe was the most affected lobe. The prevalence of post stroke epilepsy was 45.7%.

Keywords: Epilepsy; Post stroke; Prevalence; Predictive factors

Introduction

Post-stroke seizure and post-stroke epilepsy are common causes of hospital admissions, either as a presenting feature or as a complication after a stroke. They require appropriate management and support in long term. The age itself being an independent risk factor for stroke, the incidence and prevalence of post-stroke seizure and post-stroke epilepsy is likely to increase with age [1].

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Cerebrovascular disease is considered as number one cause of epilepsy in elderly. Studies found that both age specific incidence and prevalence of epilepsy are higher in older people. It is reported that the prevalence of epilepsy is as high as nearly 1% in people 85 years and over (6.98 to 8.66/1000 people) and about 11.5% of patients with stroke were at risk of developing post-stroke (delayed or late onset) seizures within five years was very similar to previous population studies [2].

Five percent are early-onset seizures (peak onset within the first day after the stroke) and another 5% are late-onset seizures-peak onset within 6 to 12 months after the stroke. Seizures develop in 3% to 4% of the stroke patients in about one third of the patients with early-onset seizures and about one half of the patients with late-onset seizures.

Clinically, it should be carefully distinguished early from late seizures. The former represent provoked seizures, occurring during the acute phases of the stroke and its immediate aftermath (up to 7 days), whereas the latter are seizures that occur after the brain has stabilized and physiological homeostasis, presumably, has been restored. Late seizures are not “provoked” by the acute events and reactions surrounding the stroke, rather they are considered unprovoked but are secondary to the static residual pathology remaining after the stroke. Repeated, unprovoked late seizures indicate epilepsy and can potentially become a life-long problem and source of disability.

There are several causes for early onset seizures after ischemic strokes. An increase in intracellular Ca²⁺ and Na⁺ with a resultant lower threshold for depolarization, glutamate excitotoxicity, hypoxia, metabolic dysfunction, global hypo perfusion, and hyper perfusion injury (particularly after carotid endarterectomy) have all been postulated as putative neurofunctional etiologies. Seizures after hemorrhagic strokes are thought to be attributable to irritation caused by products of blood metabolism [2,3].

The exact path physiology is unclear, but an associated ischemic area secondary to hemorrhages is thought to play a part. Late onset seizures are associated with the persistent changes in neuronal excitability and gliotic scarring is most probably the underlying cause. Haemosiderin deposits are thought to cause irritability after a hemorrhagic stroke. In childhood, post-stroke seizures can occur as part of perinatal birth trauma [3].

It is very difficult to predict who is likely to develop a seizure after the stroke. However, there are some known risk factors associated with a higher incidence of post-stroke seizures. Predictors include stroke severity, cortical symptoms, hemorrhages, total anterior circulation infarcts, young age at stroke, and early seizures [3].

Post-stroke seizures typically follow localization related (focal) seizure semiology, but about one third of cases present with tonic-clonic (generalized) seizures and the remaining two thirds usually present with partial seizures. Early onset seizures usually present with a focal onset while generalized tonic-clonic seizures are more common with late onset seizures. It is worth while remembering that there are atypical presentations of post-stroke seizures as well as seizure mimics; both of which can give rise to confusion and subsequent delay in appropriate diagnosis and management [3].

When CT is used in conjunction with electrolytes and EEG and clinical findings, it is a useful diagnostic tool to establish the cause of the first seizure in adults. MRI brain is the imaging modality of

choice, as it will show a number of abnormalities that may be missed on CT, for example, cortical malformations, hippocampus sclerosis, small mass lesions, and cavernomas-particularly in the temporal lobes [3,4].

EEG can be normal in about 5% of cases and, therefore, normal EEG result does not exclude epileptogenicity. Focal slowing or diffuse slowing activities are associated with a low risk of seizures whereas focal spikes, periodic lateralization, or periodic bilateral discharges are associated with a higher risk. In a prospective study with mean follow up of 15.9 months, no specific EEG pattern was found in those who later developed epilepsy [4]. Antiepileptic Drugs (AED) remain the mainstay of epilepsy management in all age groups. Single therapy controls the seizures (in 88% of cases) [4].

Throughout this context, this study is aim to measure the frequency, prevalence and predictive factors of epilepsy after stroke among Adult Sudanese Patients admitted to a number of hospitals in Khartoum state Sudan 2018.

Materials and Methods

Study design

It is a prospective multicentre hospital based study.

Study area

The study was conducted in four teaching hospitals located in Khartoum state as following (Table 1):

1. The National centre for Neurological Science
2. Omdurman Teaching Hospital
3. Bahry Teaching Hospital
4. National Ribat Teaching Hospital

All these teaching hospitals are located in Khartoum state, Sudan. They are considered as main references teaching hospital in Sudan. They provided services basically for Khartoum state area residency, and also for the general population from all over the country.

Study duration

The study was conducted in the period from November 2017 November 2018.

Study population

This study covered all patients presented to the hospital with seizure with or after stroke for admission or for follow up attended the study area based on the definition.

- Early onset seizures occur when reach a peak within 24 hr after the stroke.
- Late onset seizures occur after two weeks of stroke onset

Table 1: Sample Size.

Study area	Population*		Sampled cases	
	Number	%	Number	%
The National Centre for Neurological Science	189	41.7	58	41.7
Omdurman Teaching Hospital	105	23.2	32	23.2
Bahry Teaching Hospital	87	19.2	27	19.2
National Ribat Teaching Hospital	72	15.9	22	15.9
Total	453	100	139	100

*Source: Data obtained from medical ER

Table 2: Study variables.

Main Categories	Categories	Variable
Independent	Socio demographical	·Age
		·Sex
	Predictive factors	·Hyperlipidemia
		·Diabetes
		·Hypertension
		·Cardiac disease
		·Smoking
		·EEG
		·ECG
		·ECHO
		·Serum electrolytes
		·CT brain
		·MRI brain
		Dependent
·Type of epilepsy		
·The time from the onset of stroke to the seizures		
·Presentation		
·Treatment		

has a peak within 6 to 12 months after the stroke [3].

Inclusion criteria

1. Adults aged 16 years or more
2. Diagnosed with stroke
3. Acceptance of participation
4. Recruited from the study area within time period

Exclusion criteria

1. Patients with a history of epilepsy before stroke
2. Not fulfill for the inclusion criteria above

Data collection and methods: The data collected through a comprehensive structural close ended questionnaire. It covered all demographics and medical factors, associated factors, and frequency of epilepsy data for all study participants recruited under the study (Table 2).

Study variables

Data entry, analysis and presentation:

1. Data entered, cleaned, and analyzed using SPSS version 25.0
2. Descriptive statistics in term of frequency tables with percentages and graphs. Means and standard deviations presented with relevant graphical representation for quantitative data.
3. P value of 0.05 or less is considered statistically significant.

Ethical considerations:

1. Written permission obtained from the Administrative authority of the four teaching hospitals under the study area.
2. Study data/information used for the research purposes only. The privacy issues intentionally considered.

Table 3: Showed the distribution of gender among Sudanese patients with Epilepsy after Stroke, Khartoum State, Sudan, 2018 (n=140).

Gender	Occurrence of post stroke epilepsy				Total	
	Yes		No		No.	%
	No.	%	No.	%		
Male	30	46.9	41	53.9	71	50.7
Female	34	53.1	35	46.1	69	49.3
Total	64	100	76	100	140	100

Table 4: Showed the distribution of age in years among Sudanese patients with epilepsy after Stroke, Khartoum State, Sudan, 2018 (n=140).

Age (years)	Occurrence of post stroke epilepsy				Total	
	Yes		No		No.	%
	No.	%	No.	%		
16 - 30	6	9.4	2	2.6	8	5.7
30 - 60	17	26.6	18	23.7	35	25
> 60	41	64.1	56	73.7	97	69.3
Total	64	100	76	100	140	100

3. The participation is voluntary. Any participants have own right to stop at any stage.
4. Written informed consent obtained from all participants.

Results

Gender and age distribution

This study covered 140 study participants, with almost equal gender ratio male: female 1:1 and more than two thirds 69.3% of them were above 60 years of age as showed in (Table 3).

Distribution of post stroke epilepsy according to age and gender

30 (46.9%) were males and 34 (53.1%) were females. Moreover,

Table 5: Showed the distribution of stroke risk factors among Sudanese patients with epilepsy after Stroke, Khartoum State, Sudan, 2018 (n=140).

Stroke risk factors	Occurrence of post stroke epilepsy				Total	
	Yes		No		No.	%
	No.	%	No.	%		
Hypertension	42	65.6	41	53.9	83	59.3
Diabetes	35	54.7	15	19.7	50	35.7
Smoking	3	4.7	9	11.8	12	8.6
Hypercholesterolemia	4	6.3	4	5.3	8	5.7
Coronary heart disease	6	9.4	8	10.5	14	10
Atrial fibrillation	5	7.8	7	9.2	12	8.6

out of 64 patients with post stroke epilepsy, the study found that 6 (9.4%) of them were 16 to 30 years of age, 17 (26.6%) were 30 to 60 years of age and 41 (64.1%) were more than 60 years as detailed in (Table 4).

- Risk Factors for Stroke
- Forty two 42 (65.6%) had hypertension, 35 (54.7%) diabetes, 3 (4.7%) had smoking, 4 (6.3%) with Hypercholesterolemia, 6 (9.4%) with CHD and 5 (7.8%) with Atrial fibrillation as detailed in (Table 5).
- Seizures Characteristics

Prevalence of post-stroke seizures

The prevalence of post stroke seizures among the study participants was 45.7%, with equal ratio between early and late onset 1:1.

Type of epilepsy

The most frequent types were generalized tonic clonic 54.7%, simple partial 10.9% then focal with secondary generalization 17.2%.

Lobar affection and frequency

Parietal lobe was affected in 37.5%, frontal lobe in 12.5% and multiple lobar affection in 17.5%, as detailed in (Table 6).

Clinical Findings

Cranial nerves

More than half 56.4% of the study participants were oriented, only 51.4% had affected cranial nerves, mainly the 7th among 47.2%, while 9th and 10th among 26.4 % of them, more than half of the had weakness on the left side 52.9% as detailed in (Table 7).

Investigations

MRI findings, EEG, ECG and Echo

Brain MRI & MRA Showed parietal lobe affection in 37.5%, frontal lobe in 12.5% and multiple lobar affection was found in 17.5%. Only 1.4% had poly spikes waves in EEG, 21.5% atrial fibrillation in ECG, 2.9%, in Echocardiography 26.4% had cardiac thrombus, 9.3% had valve disease, and finally 20.7% had blood glucose more than 200 mg/dl (Figure 1-4).

Electrolytes and renal function tests

High potassium was found in 3.6%, low sodium in 2.9%, low calcium in 5%, low magnesium 3.6%.

High urea in 16.4% and high creatinine in 15% as detailed in (Figure 5).

Stroke Type

Twenty percent (20%) had intracranial hemorrhage, 80% had ischemic stroke. The main finding in ischemic stroke was MCA in 88.9%, and similar ratio was found in intracranial hemorrhage as lobar localization and Deep localization as detailed in (Figures 6-8).

Table 6: Showed the distribution of seizures characteristics among Sudanese patients with epilepsy after Stroke, Khartoum State, Sudan, 2018 (n=140).

	Seizures characteristics		Frequency	Percent
	Yes	No		
Frequency of PSS	Yes		64	46
	No		76	54
Seizures onset (n=64)	Early onset seizures	Within one week after the stroke	22	34
		One week after the stroke	10	16
	Late-onset seizures within 6 to 12 months after the stroke	32	50	
Seizures Type (n=64)	Generalized tonic clonic		35	55
	Simple partial		7	11
	Complex partial		6	9.4
	Myoclonic		2	3.1
	Focal with secondary generalization		11	17
	Mixed		3	4.7
Lobar affection (n=64)	Temporal		15	23
	Frontal		8	13
	Parietal		24	38
	Occipital		6	9.4
	Multiple		11	17
Seizures Frequency (n=64)	Single		17	27
	Multiple		41	64
	Convulsive status		6	9.4

Table 7: Showed the distribution of clinical findings among patients with epilepsy after Stroke among adult Sudanese Patient, Khartoum State, Sudan, 2018 (n=140).

Clinical findings	Frequency		Percent	
GCS	<9	29	20.7	
	>9	32	22.9	
	Oriented	79	56.4	
Cranial nerves	Affected	72	51.4	
	Not affected	68	48.6	
If affect what cranial nerve are affected (n = 72)	1 st	0	0	
	2 nd	0	0	
	3 rd	0	0	
	4 th	0	0	
	5 th	0	0	
	6 th	0	0	
	7 th	34	47.2	
	8 th	0	0	
	9 th	19	26.4	
	10 th	19	26.4	
	11 th	0	0	
	12 th	0	0	
Side of the weakness	Left side	74	52.9	
	Right side	66	47.1	
Power	G0	75	53.3	
	G1	19	13.6	
	G2	23	16.4	
	G3	17	12.1	
	G4	3	2.1	
	G5	3	2.1	

Table 8: The relation between the Type of stroke with the Occurrence of Post stroke seizures among patients with epilepsy after Stroke among adult Sudanese Patients, Khartoum State, Sudan, 2018 (n = 140).

Type of stroke		Occurrence of Post stroke seizures				Total	
		Yes (n=64)		No (n=76)		Freq.	Percent
		Freq.	Percent	Freq.	Percent		
ICH		22	68.8	10	31.3	32	100
	Ischemic	42	38.9	66	61.1	108	100
Total		64	45.7	76	54.3	140	100

$\chi^2=8.870$, P value=0.0029

Treatment

The patient had been treated using Diazepam 11.4%, Phenytoin 25.7% and Carbamazepine 20% and other set of medicines detailed below, while they took aspirin 49.3%, Atorvastatin 49.3% and Warfarin 4.3% for stroke treatment.

Cross Tabulation

Cross tabulation was done to assess the possible relationship between the type of the stroke and the occurrence of Post stroke seizures among the study participants using chi squared statistical test. The result found that there is a significant association between them (p value =0.0029). It is noticed that being diagnosed as hemorrhagic stroke considered as the main predictive factors for the future occurrence of Post stroke seizures.

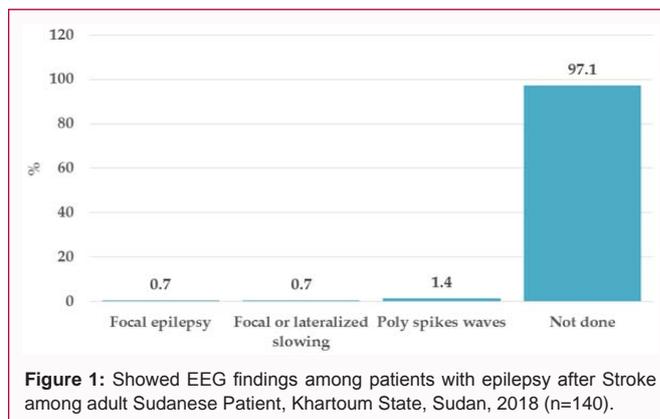


Figure 1: Showed EEG findings among patients with epilepsy after Stroke among adult Sudanese Patient, Khartoum State, Sudan, 2018 (n=140).

Discussion

This study aimed to measure the frequency and predictive factors for post stroke epilepsy among adults in Khartoum state, Sudan, 2018. This study covered 140 study participants, with almost equal gender ratio male: female 1:1 and more than two thirds 69.3% of them were above 60 years of age. 30 (46.9%) were males and 34 (53.1%) were females had post stroke epilepsy and 41 (64.1%) were more than 60 years.

The most common risk factors was hypertension in 42 (65.6%) followed by diabetes in 35 (54.7%).

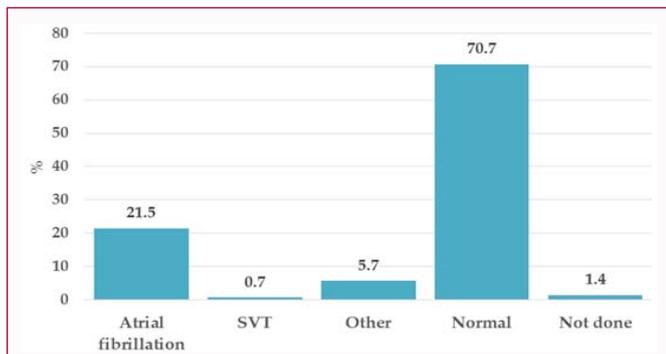


Figure 2: Showed the ECG findings among patients with epilepsy after Stroke among adult Sudanese Patient, Khartoum State, Sudan, 2018 (n=140).

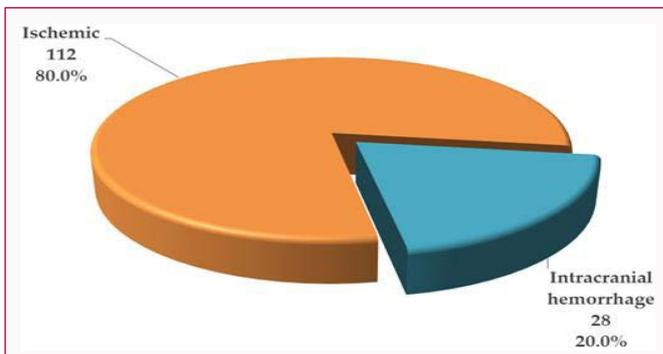


Figure 6: Showed the distribution of Type of stroke among patients with epilepsy after Stroke among adult Sudanese Patient, Khartoum State, Sudan, 2018 (n=140).

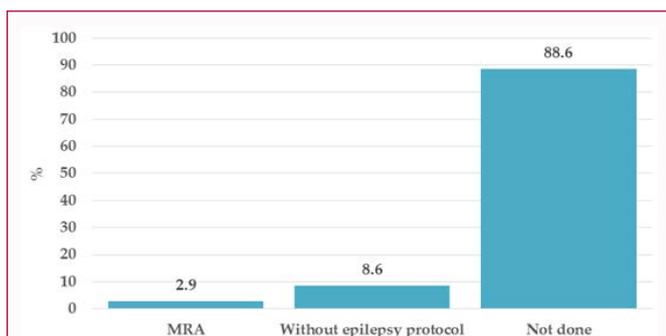


Figure 3: Showed-MRI findings among patients with epilepsy after Stroke among adult Sudanese Patient, Khartoum State, Sudan, 2018 (n=140).

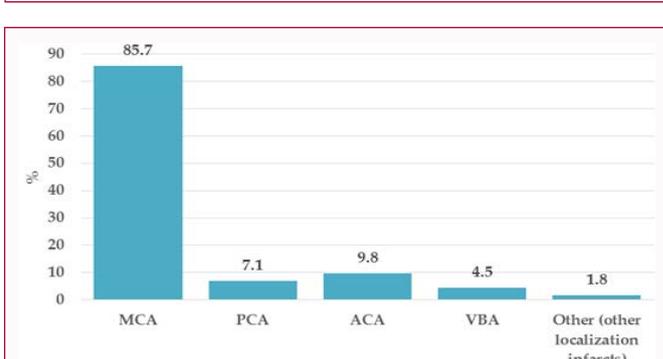


Figure 7: Showed the distribution of Type of Ischemic stroke among Sudanese patients with epilepsy after Stroke, Khartoum State, Sudan, 2018 (n=112).

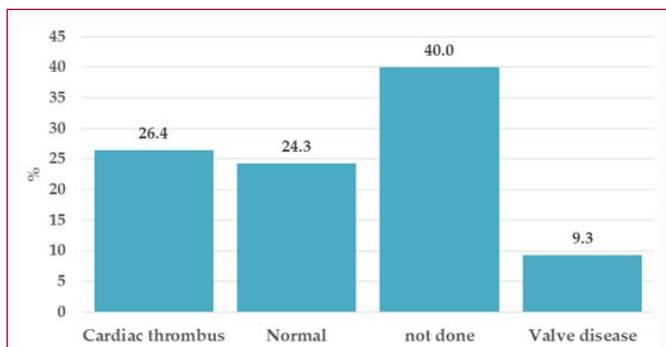


Figure 4: Showed the Echocardiography among patients with epilepsy after Stroke among adult Sudanese Patient, Khartoum State, Sudan, 2018 (n=140).

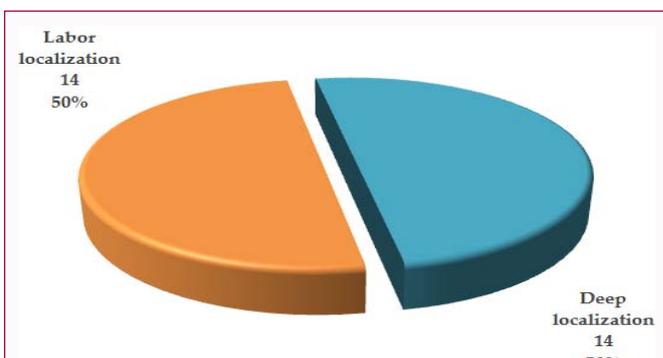


Figure 8: Showed the distribution of Type of Intracranial hemorrhage among Sudanese patients with epilepsy after Stroke, Khartoum State, Sudan, 2018 (n=28).

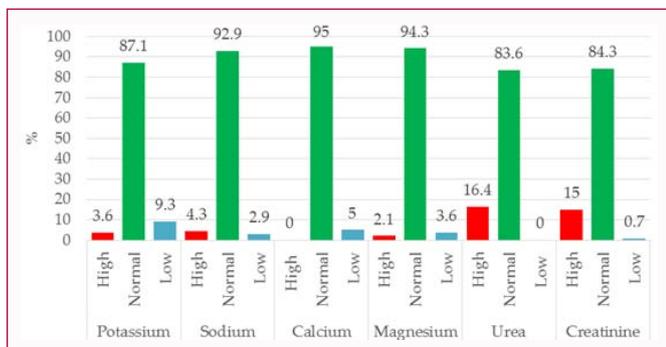


Figure 5: Showed the distribution of their Electrolytes and renal function among patients with epilepsy after Stroke among adult Sudanese Patient, Khartoum State, Sudan, 2018 (n=140).

The study found that the prevalence of post stroke seizures among the study participants was 45.7%, with equal ratio between

early and late onset 1:1. Similarly, other study from Thailand found that the time from the onset of stroke to the seizures was mostly in (60.3%) less than 2 weeks (i.e., early post-stroke seizures) [5]. Other Indian study found that among the whole group with stroke, early onset seizures were seen in 22 (1.8%) patients and 10 patients (0.8%) developed status epilepticus [6]. The frequency of post stroke seizures in our study was not in favour with Italian study who found that only (4.8%) had post stroke seizures [7]. In Germany the researcher stated that following stroke, 3% to 6% of patients develop acute symptomatic seizures within the first 7 days [8].

Other studies found that approximately 50% to 90% of early onset seizures appear to be simple partial seizures [9].

In this study the most frequent types of seizures were generalized

tonic clonic 54.7%, simple partial 10.9% then focal with secondary generalization 17.2%, while parietal lobe was affected in 37.5%, frontal lobe in 12.5% and multiple lobar affection in 17.5%. In other relevant Indian study [6] found that 17.9% of patients had cardiogenic embolism in addition, 34% of patients had partial seizures with or without generalization whereas 33% of patients had generalized tonic clonic seizures without partial onset. Several studies established cortical location, stroke severity, cardio-embolic stroke and hemorrhagic infarction as common risk factors of post ischemic stroke seizures [9].

The study found that more than half 56.4% of the study participants were oriented, only 51.4% had affected cranial nerves, mainly the 7th among 77.8%, and the 10th among 33.3% of them, more than half of the patients had weakness within the left side 52.9% while 95.4% of them had power less than G4.

The study found that 20% of study participants had intracranial hemorrhage, 80% had ischemic stroke. The main finding in ischemic stroke was MCA in 88.9%, and similar ratio was found in intracranial hemorrhage between lobar localization and Deep localization. Other Indian study found simpler results Fifty % had anterior circulation stroke (middle cerebral 46%, anterior cerebral 3%, internal carotid 1%), while 25% patients had posterior circulation stroke and three had border zone infarct [6].

Regarding the treatment, the patient had been treated using Diazepam 11.4%, Phenytoin 25.7% and Carbamazepine 20% and other set of medicines detailed below, while they took aspirin 49.3, atorvastatin 49.3 and warfarin 4.3% for stroke treatment. In Indian study [6] Seizures were controlled with single antiepileptic medication in 40 patients; two drugs in 21 and five required multiple drugs.

Cross tabulation was done to assess the possible relationship between the types of the stroke with the occurrence of Post stroke seizures among the study participants. The result found that there is a significant association between them (p value =0.0029) (Table 8). It is noticed that being diagnosed as hemorrhagic stroke considered as main predictive factors for the future occurrence of Post stroke seizures. This result was in agreement with the Nigerian study that found that the study found that EPASS occurred in 9.96% of subjects and intracerebral infarct was more associated with EPASS, a finding different from what is dominant in western literature [6]. While other study from Thailand found that associated factors of post-stroke seizures were also intracerebral hemorrhage (p=0.015), and lesions at cortical area (p=0.05) [5].

In American study they found similar result that an independent risk factors for seizure development included hemorrhagic stroke [10]. They add additional concern regarding Race/ethnicity or localization of the ischemic stroke did not influence the risk for seizure development in the studied population [10]. In Italian study they also found that Seizures were significantly more common in patients with severe and large stroke, and in patient with hemorrhagic stroke [7] in German study they concluded that the rate is higher after cerebral hemorrhage compared to ischemia [11].

The study had some limitations. The relatively limited number of study participant (140 only) may affect negatively the probability of founding significant relationships between different modes and feeding with the overall incidence of PSS among Sudanese patients.

Another limitation, follow up. Some outcomes-such as long term outcome or the presence of long term complication - may need to be followed overtime for longer period. So, a long term prospective cohort follow up design may be useful for more detailed description for the practices towards PSS among this important risky group.

Conclusion

The study found that the frequency of post stroke seizures among the study participants was 45.7%, with equal ratio between early and late onset. Most of them were with age more than sixty years. There was a significant association between post stroke seizures and hemorrhagic stroke. This considered as a main predictive factors for the future occurrence of Post stroke seizures. Hypertension followed by Diabetes was the main risk factors followed by cardiac thrombus and atrial fibrillation. Generalized seizures were common. The parietal lobe was the most affected lobe.

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