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ORIGINAL ARTICLE

CAREGIVER REPORTED INCIDENCE OF STATUS EPILEPTICUS IN PERSONS WITH EPILEPSY IN ENUGU, SOUTHEAST NIGERIA.

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ABSTRACT

Background: *Status epilepticus is a neurological emergency which may occur in people with epilepsy. Ascertaining the incidence of status epilepticus in the community is wrought with many challenges and few reports exist in sub–Saharan Africa, a region with a high burden of epilepsy.*
Objective: *The aim of this study was to describe reported incidence of status epilepticus among epilepsy patients attending neurology outpatient clinic in Enugu.*
Methods: *This was cross-sectional study carried out in the medical out-patient clinics in Enugu Nigeria. Data were collected using a semi-structured questionnaire. Informants were patients and their caregivers. Status epilepticus defined as seizures based on International League Against Epilepsy criteria.*
Results: *Data of 154 patients were reviewed and analysed. A total of 56(36.4%) confirmed that they had experienced seizures that could be described as status epilepticus (males (36.3%) and females (36.5%)). P=0.98. About 54.5% of those with stroke and 47.9% of patients who had cluster seizures reported a history of status epilepticus. Factors that correlated with having status epilepticus were history of cluster seizures, family history of epilepsy and having no past history of seizure related admissions.*
Conclusions: *The reported incidence of status epilepticus among epilepsy patients attending tertiary hospital clinics in Enugu is high. Factors that may account for this includes, non-adherence, or greater seizure severity. Careful patient education will improve emergency management of epilepsy to reduce the morbidity related to epilepsy in the community.*
Keywords*: Status Epilepticus, Cluster seizures, Epilepsy, Nigeria.*

INTRODUCTION

Status epilepticus (SE) is a neurological emergency which may occur in people with epilepsy (PWE) as well as in those without epilepsy. It is associated with high morbidity, mortality and low quality of life thus in PWE episodes of SE have added clinical relevance (1,2). In 2015, the International League Against Epilepsy defined SE as a bilateral tonic–clonic activity lasting longer than 5 minutes, and absence SE and as focal SE as exceeding 10 minutes (3). Because of the time-locked definition of SE ascertaining the incidence of SE in the community is wrought with many challenges (4) thus most available studies are hospital based. In a review of population-based studies, Sanchez et all (4) reported an overall incidence of SE 9.9 to 41 per 100,000/year ranging from 3.5 to 41 per 100 000 per year. Recent studies from Europe have reported incidence rate of 36.1 to 81.1 per 100 000 per year based on the new ILAE 2015 definition of SE(5,6).

Few studies have reported on SE in Africa(7,8). Bhalla et al (7) in 2014 reported an incidence of 10.8 per 100 000 population and Kariuki et al (8) reported a prevalence rate of 2.3 per 1000. Apart from using different definitions for SE, these studies included people without epilepsy and children. Based on few available studies in SSA, SE in Africa is reported to be high in Children, hospital-based studies and PWE who are not on antiepileptic drugs (9,10). Most cases of documented SE are likely to be seizures with predominantly motor features. In Austria, the age and sex adjusted incidence of a first episode of non-convulsive SE and SE with prominent motor phenomena was 12.1 and 24 per 100 000 adults per year, respectively (5).

In Sub-Saharan Africa (SSA), risk factors for SE include infections and non-adherence to medication. In Kenya, for example, documented risk factors for SE were neurologic impairments, acute encephalopathy, previous hospitalization, and presence of antibody titers to falciparum malaria and HIV (8). Risk factors for SE and seizure clusters seizure (SC) have been reported to be similar (11,12). SE is a strong determinant of quality of life in PWE/their caregivers and the cost of treating epilepsy (1,13,14) . In SSA, SE may be treated at home and possibly in unorthodox way which may result in high morbidity and mortality.

Despite the potential for poor outcomes of SE in PWE, there is little, or no research related to the subject in Nigeria. Recognizing incidence and patterns of SE is helpful in preventing untoward consequences of SE. The aim of this study was to describe the caregiver reported frequency and pattern of SE in PWE attending neurology outpatient clinic in Enugu.

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METHODS

This was a cross-sectional descriptive study carried out in 3 major hospitals in the city of Enugu, Enugu State Nigeria. The Hospitals were the University of Nigeria Teaching Hospital, Enugu State University Teaching Hospital, and the Memfys Hospital for Neurosurgery. These three tertiary hospitals offer both secondary and tertiary epilepsy care in the city and receive patients from all parts of southeast Nigeria and beyond.

Study participants **:**The plan was to collect the data of all consecutive consenting epilepsy patients who attend the neurology clinic of these hospitals. All consecutive consenting patients accompanied by caregivers in which case the caregiver must have been an eyewitness of the seizure were included in the study. We excluded patients with possible psychogenic non-epileptic seizures and single epileptic seizures. Cases where seizure duration could not be truly determined with some level of certainty were excluded from the present analysis. Cases of incomplete data or illegible lasting less than 5 minutes were also excluded. The study period was 9 months.

Data collection tools and procedures: Data was collected using a semi-structured questionnaire. The questionnaire contained open ended and as well as multiple choice questions and consisted of three principal sections. The first section was on general information about the respondents such as age and sex and related characteristics. The second section contained questions on the age on onset of epilepsy, age of first treatment and family history. The third section was focused on clinical characteristics of seizures such as prediction of seizures, seizure triggers, duration of seizures in minutes or recurrent seizures during which the patients did not recover consciousness. The questionnaire was constructed in simple English to match the expected reading level of most persons that completed primary school (6 years of basic education). Cues to remember seizure duration were given to informants. Such cues include questions like (1) do you think that seizures lasted as long as the time you have been in this clinic? (2) did seizures last as long as it took you to get to a hospital or call for help? The study questionnaire was designed by the principal investigator and reviewed by the other authors and senior colleagues in neurology both in Enugu and outside. The mean time for filling out the questionnaire was 5 minutes. All questionnaires were filled in the English language either by the caregiver (self-administered) and sometimes with help from the investigators. Data were collected by neurology registrars, senior registrars and consultants.

Completed questionnaires were retrieved the same day. In cases where the respondent did not understand English, a translation in the local language was used. In such cases, the items on the questionnaire were read out to the respondents, and their endorsed options were ticked by the investigator. The study protocol was reviewed by the ethics committee of the Teaching Hospitals. All participants gave their informed consent after reading or having the consent form read for them.

Operational definitions: SE was defined as seizures lasting more than 5 minutes for generalized seizures and 10 minutes for focal seizures3. CS was defined as series of seizures closely grouped in time with shorter than normal inter ictal periods or as an increase over the patient's typical seizure frequency in a day or week (15). Epilepsy was defined based on the International League Against Epilepsy criteria.

Data analysis: The SPSS version 22 (IBM Corporation, New York, USA) was used for data management and statistical analysis. Data were presented in tables. The statistical methods included Mann-Whitney U test for unpaired observations and Chi-squared test for comparison of categorical data. Distribution of types of seizures was calculated as the percentage of participants. Mean and median were calculated, and values were presented as tables where applicable. In all, $p < 0.05$ was regarded as statistically significant. Conclusions were drawn at this level of significance at 95% confidence level.

RESULTS

Description of participants: Data of 154 PWE were reviewed and analysed. Males were 80(51.9%) and 74(48.1%) were females. The male to female ratio was 0.9:1. Most participants were aged 20-29 years (42.9%) with a mean age of 32.4(17.3) years. Males were older than females by almost 7 years ($p<0.0$). Other characteristics of the patients are shown in Table 1. Before presenting to the hospital 40(26%) used traditional herbal drugs while 36(23.4%) resorted to prayer as a sole means of treatment.

Seizure characteristics: Reported seizures characteristics are shown in Table 2. The mean age of onset of epilepsy in the cohort was 20.9 years (with a median of 17 years); earlier in females (14.4 years) than males 26.3 years) ($p <0.01$). The peak age of onset of epilepsy in SE was 0 to 9 years. The mean time taken from the age of onset to the age of going to the hospital was similar in both males and females. P=0.2. The 6-month seizure freedom was 9.7%. More males reported a family history of epilepsy. P=0.03. About 45.5% reported a clinical history of generalized seizures. Among those that had focal seizures clinically, 38(45.2%) could always predict the onset of seizures while the rest did so sometimes. Clinically seizures were reported to be similar every time by 107 (69.5%).

Table 1. Age and gender distribution Patients' demographic and clinical characteristics.

Gender	**Male (%)**	**Female (%)**	**Total (%)**	**p-value**
N (%)	80(51.9)	74(48.1)	154(100)	0.63
Age (years)				
Mean age (sd)	35.8(18.9)	28.7(14.5)	32.4(17.3)	0.01
Median age	29.5	28.7	26	
Age group				
< 20	11(13.8)	14(18.9)	25(16.2)	
20-29	29(36.3)	37(50)	66(42.9)	
30-39	15(18.8)	13(17.6)	28(18.2)	
40-49	8(10)	3(4.1)	11(7.1)	
≥50	17(21.3)	7(9.5)	24(15.6)	0.1
Level of education				
No education	15(18.8)	4(5.4)	19(12.3)	
Primary	13(16.3)	9(12.2)	22(14.3)	
Junior secondary	6(7.5)	14(18.9)	20(13)	
Senior secondary	30(40.7)	32(43.2)	62(40.3)	
Tertiary	16(20)	15(20.3)	31(20.1)	0.04
Occupation				
Students	17(21.3)	28(37.8)	45(29.2)	
Employed	37(46.3)	31(41.9)	68(44.2)	
Unemployed	17(21.3)	13(17.6)	30(19.5)	
Retired	9(11.3)	2(2.7)	11(7.1)	0.05
Substance use				
Alcohol use	22(27.5)	6(8.1)	28(18.2)	<0.01
Tobacco	11(13.8%)	3(4.1)	14(9.1)	0.04
Marijuana	5(6.3)	-	5(3.2)	0.03
Glue	-	1(1.4)	1(0.6)	0.3
Alternative treatment				
Herbal	25(31.3)	15(20.3)	40(26)	0.12
Prayer house	16(20)	20(27)	36(23.4)	0.3
Drug store	7(8.8)	3(4.1)	10(6.5)	0.24

Table 2. Gender distribution of seizure characteristics

Gender	Male (%)	Female (%)	Total (%)	p-value
Age of onset				
Mean age (sd)	26.3(21.7)	14.4(14.9)	20.9(15.3)	<0.01
Median age	18	12	17	
Time taken before first hospital visit (years)				
Mean age (sd)	1.6(4.5)	2.7(5.3)	2.1(0.4)	0.2
Median (range)	0(0-28)	0(0-21)	0(0-28)	
Last seizure episode				
< 24 hours	18(22.5)	20(27)	38(24.7)	
1-7 days	18(22.5)	16(21.6)	34(22.1)	
1-4 weeks	16(20)	12(16.2)	28(18.2)	
1-6 months	21(26.3)	18(24.3)	39(25.3)	
>6 months	7(8.8)	8(10.8)	15(9.7)	0.97
Family History	16(19.8)	5(7.2)	21(14)	0.03
Prediction of seizures				
Always	21(26.3)	17(23)	38(24.7)	
Sometimes	17(21.3)	29(39.2)	46(29.9)	
Never	42(52.5)	28(37.8)	70(45.5)	0.05
Seizures are similar	54(67.5)	53(71.6)	107(69.5)	0.58
History of status epilepticus	29(36.3)	27(36.5)	56(36.4)	0.98
Seizure related admissions	3(3.8)	11(14.9)	14(9.1)	0.02*
Total	80(51.9)	74(48.1)	154(100)	

*Mann-Whitney U Test.

A total of 56(36.4%) confirmed that they had experienced prolonged seizures that lasted more than 5 minutes for generalized seizures and 10 minutes for focal seizures in the past. Sex distribution SE showed that males (36.3%) and females (36.5%) reported a history of status in the past. P=0.98. Seizure related admissions were reported in 14(9.1%) of PWE more in females 11(14.9%) than males 3(3.8%). See Table 3. Figure 1, showed that history of SE appears to be bimodal; 40% below the age of 20 years and 50% after the after of 50 years.

Table 3 shows the proportion of PWE with various risk factors who had SE. About 54.5% of those with stroke, 47.9% of patients who had CS reported a history of SE. A large proportion of dementia cases also had CS and SE although the overall number was small. Factors that correlated with past history of SE were: history of CS, family history of epilepsy and having no past history of seizure related admissions.

Table 3. Distribution of status epilepticus by various documented risk factors

Risk factor	N(%)	Status N(%)#
No risk factor	84(54.5)	28 (33.3)
Cluster seizures	73(47.4)	35(47.9)
Traumatic brain injury	34(22.1)	12(35.3)
Stroke	11(7.1)	6(54.5)
Alcohol abuse	5(1.9)	1(20)
Mental retardation	4(1.9)	-
Dementia	4(2.6)	3(75)
Meningitis	3(1.3)	2(66.7)
Migraine	3(1.9)	1(33.3)
AIDS	3(0.6)	-
Brain surgery	2(2.6)	-
Down's syndrome	1(3.2)	1(100)
Psychosis	1(0.6)	-
Hypertension	20(13.3)	10(18.5)
Diabetes	5(3.2)	1(20)
Heart failure	1(0.6)	-
Total	154(100)*	54(36)

*Multiple risk factor was recorded.
#Percentage of risk factors.

Table 4. Correlates of status epilepticus. Table 4. Correlates of status epilepticus.

	Status Epilepticus r (p-value)
Gender	
Status epilepticus	-
Seizure cluster	23(<0.01)
Age	-0.02(0.84)
Gender (1 male, 2 female)	-0.00(0.98)
Family history	0.17(0.03)
Age of onset of epilepsy	0.12(0.15)
Seizure type (1 generalized, 0 focal)	0.01(0.74)
History injuries (1 yes, 2 No)	0.12(0.15)
Seizure related admissions (1 yes, 0 No)	-0.23(<0.01)
First point of care (0 hospital, 1 other places)	0.04(0.59)
Seizure semiology (1 similar, 0 varies)	-0.03(0.74)
Last seizure (1 less than 24 hours to 6 greater than 6 months)	0.09(0.29)

DISCUSSION

Seizure frequency and pattern are strong determinants of quality of life in epilepsy as well as the burden of epilepsy. Although in PWE, seizures are generally sporadic or even infrequent, however, they may experience prolonged seizures (status epilepticus) and even cluster seizures. Identification of SE in the community is very important because of the associated high morbidity, mortality as well as the associated high direct and indirect health costs in epilepsy(13,14).

In the index study, the male to female ratio of PWE with a history of SE was 0.9:1. SE was reported by 36.4%: males (36.3%) and females 36.5%). P=0.98. About 54.5% of PWE who had stroke experienced SE. A large proportion of dementia cases also had SE although the numbers were small. Furthermore, the age distribution of SE was bimodal (before 20 years and after 50 years), and a large proportion of PWE with SE also had experienced SC. Factors that correlated with SE were history of SC, family history of epilepsy and no history of seizure related admissions.

The seizure related characteristics in the index study were similar to other published works from Nigeria (16,17). The age distribution of the patients in the index study may suggest a changing pattern of epilepsy risk factors or increasing awareness of epilepsy in the country. Younger mean-age-of-onset in females may be attributed to a better health seeking behaviour among females. Another factor responsible for this may be relatively large proportion of individuals with hypertension, diabetes and stroke. These disorders are generally commoner in older males. Clinically, 54.5% had focal seizures, a finding which may be explained by the high rates of risk factors for focal seizures in the study. This is similar to previous studies (18). Six-month seizure freedom in the index study was a mere 9.7% while 24.7% reported within 24 hours of seizures. These findings support previous reports on seizure control in PWE in Nigeria(17). These may be related to several factors including non-adherence, uses of unorthodox medicine, seizure severity and alcohol (18).

The sex and age distribution of PWE who reported a history of SE showed same sex distribution and a bimodal age distribution. In the US, Dham et al(19) reported a bimodal distribution of SE with the first peak in the first decade of life and the second after 60 years. Double peak in the incidence of SE was also reported in a review by Sanchez et al(4). Current demographic in Nigeria and SSA have shown a rise in the older age group; therefore, SE is likely to become a common problem and an important health issue in years to come. Similar to some previous studies, the gender distribution of SE has been reported to be similar in males and females. Male to female ratio varied also from one study to the other with some reporting more males and others more females (4). In Ethiopia, Amare et al(20) reported a male-to-female ratio of SE of 1.5:1 which is different from the index study. In a study by Kariuki et al (8) there was an equal gender distribution.

There are no community-based studies on SE in Nigeria. Community-based studies are frequently limited by recall bias and the ability of onlookers to recognize seizure-types and record their duration appropriately. Even in hospital settings in Nigeria, EEG monitory is not frequently carried out hence there are likely to be low rates of detection.

The definition of SE has evolved over the past decades, however, the incidence of SE has not differed much using different definitions. Leitinger et al (5) reported that reducing the diagnostic time of SE increased the incidence only moderately by 10%. The overall incidence of SE range from 5.2 to 41 per 100,000/year (7) with an average of 9.9 per 100 000. Kantanen, et al (6) reported an annual age-adjusted incidence of 81.1/100,000 based on the new ILAE 2015 definition of SE.

The age and sex adjusted incidence of a first episode of SE, Non-convulsive statue epilepticus and SE with prominent motor phenomena (including Convulsive SE) was 36.1 per 100 000 adults per year in Austria (5). In SSA, Kiruiki and his colleagues reported an overall prevalence of 2.3 per 1,000 from three sites in Kenya(8). Their study included children and were limited to predominantly motor seizures and people without epilepsy. The reported incidence of SE in the index study (36.3%) is similar in males and females. This finding is within the rates reported by previous studies. The prevalence of SE in this study may be affected by several factors listed in table 4 which have been linked to SE in previous studies. Furthermore, our cohort may represent patients with severe forms of epilepsy.

The incidence of SE is affected by age, geographical location, comorbidities and possibly family history (6,21). Similar to the index study in most adult studies there is a spike after the age of 50 (5,22). Geographical factors affect socio cultural characteristics of the population as well as disease pattern(4). For an example, whereas in Kenya (8), Malaria and HIV were associated with SE, in Finland (6) alcohol withdrawal was the single most common acute symptomatic etiology in the study by Kantenen et al (6,23). The relationship between SE and non-adherence and no previous hospital visit have also been documented in PWE(8). These two factors are important in SSA because large treatment gap and poverty.

In the index study, SE was reported in 54.5% of those with a history of stroke and 35.3% of those with Traumatic Brain Injury (TBI). Other cases with small but significant proportion of SE were those with meningitis and alcohol abuse. These findings are in support of previous studies that reported stokes, TBI and infections as common causes of SE a pattern which tends to vary between countries (4). SE has also been reported to be common in neurodegenerative disorders (4). African studies have reported infections and non-adherence to be high on the list of risk factors(8-10,20). Sadarangani et al(10), in Kenyan children, found that 71% of SE cases had an infectious cause, 53% attributed to malaria. Likewise, Amare et al (20) described CNS infections as the primary source of SE in Ethiopia. However, these studies were not limited to PWE. SE may also be related to the premorbid state of the patients (4,24,25). Metabolic disorders such as hyperglycemia, uremia and acidosis of other etiologies are common causes of SE in non-epilepsy patients and may trigger status in PWE. Another risk factor for SE reported in the literature is family history.

In a population-based twin study reported a high pattern of SE concordance between monozygotic twins compared to dizygotic twins, linking familial predisposition and possible genetics factors to the risk of developing SE(25). Family history of epilepsy was reported in 14% of our cohort and correlated to a history of SE in the index study.

Factors that may precipitate/cause SE can also precipitate SC. These risk factors include TBI, longer duration of epilepsy and poor seizure control(26). SE has a direct effect on mortality, quality of life and increased health cost. It leads to repeated admissions in the emergency room or even in the intensive care unit. In the index study seizure related admissions negatively correlated to a history of SE. The reason for this is not clear. Large prospective studies are needed to shed more light on this finding. SE is a condition for which data on incidence, etiology, risk factors and outcomes are required for proper decision-making and for the allocation of resources by policy makers. These resources need to be used in the development of strategies that help improve prevention, diagnosis and reduce morbidity and mortality.

Limitations: This study has some limitations. Firstly, data used in this might have been affected by recall bias which may affect the true incidence of SE. Secondly, the timing of seizures may not be very accurate and subjective. Thirdly, only predominately motor seizures are observable, and subtle form of seizure are likely to be overlooked. Our study addressed only survivors. Mortality rates of SE are important in assessing the true burden of this complication of epilepsy.

Finally, questionnaires were administered in English which may introduce some language bias because some medical terms in English do not have direct local equivalents. These limitations notwithstanding, this study has provided data for comparison for future studies. Large multi-center and community-based studies are needed to accurately document the prevalence of SE in Nigeria.

Conclusion: The reported lifetime history of SE among PWE attending a tertiary hospital clinic in Enugu is high. This may suggest both poor seizure control and/or seizure severity. Careful patient education will improve both adherence and emergency management of epilepsy to reduce the morbidity of epilepsy in the community.

REFERENCES.

1. Scott RC, Surtees RAH, Neville BGR. Status epilepticus: pathophysiology, epidemiology, and outcomes. *Arch Dis Child* 1998;79:73–77.
2. Penovich P, A Clinical Update on the Importance of Recognizing Seizure Clusters. https://www.medscape.org/viewarticle/863062
3. Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, et al. A definition and classification of status epilepticus–report of the ILAE Task Force on classification of status epilepticus. Epilepsia 2015;56:1515–23.
4. Sánchez S, Rincon F. Status Epilepticus: Epidemiology and Public Health Needs. J. Clin. Med. 2016, 5, 71
5. Leitinger M, Trinka E, Giovannini G, Zimmermann G, Florea C, Rohracher A et al. Epidemiology of status epilepticus in adults; population based study on incidence, causes and outcomes. Epilepsia 2019;60:53–62.
6. Kantanen A-M, Sairanen J, Kälviäinen R, Incidence of the different stages of status epilepticus in Eastern Finland: A population -based study, Epilepsy & Behav. , 2019;29:106413.https://doi.org/10.1016/j.yebeh.2019.07.014
7. Bhalla D, Tchalla AE, Mignard C, et al. First-ever population-based study on status epilepticus in French Island of La Reunion (France) - incidence and fatality. Seizure. 2014; 23:769–773.

8. Kariuki SM, Kakooza-Mwesige A, Wagner RG, Chengo E, White S, Kamuyu G, et al. For the SEEDS Writing Group. Prevalence and factors associated with convulsive status epilepticus in Africans with epilepsy Neurology 2015; 84;(5): 1838-1845
9. Newton CR, Kariuki SM. Status epilepticus in sub-Saharan Africa: new findings. Epilepsia 2013;54(6):50–53.
10. Sadarangani M, Seaton C, Scott JA, Ogutu B, Edwards T, Prins A et al. Incidence and outcome of convulsive status epilepticus in Kenyan children: a cohort study. Lancet Neurol 2008;7:145–150.
11. Haut SR. Seizure clustering. Epilepsy Behav. 2006;8:50-55.
12. Haut SR, Shinnar S, Moshé SL, O'Dell C, Legatt AD. The association between seizure clustering and convulsive status epilepticus in patients with intractable complex partial seizures. Epilepsia. 1999;40:1832-1834.
13. Horváth L, Fekete I, Molnár M, Válóczy R, Sándor M, Fekete K. The Outcome of Status Epilepticus and Long-Term Follow-Up Frontiers in Neurology. 2017; 10:427 doi: 10.3389/fneur.2019.00427
14. Penovich PE, Buelow J, Steinberg K, Sirven J, Wheless J, Burden of Seizure Clusters on Patients With Epilepsy and Caregivers Survey of Patient, Caregiver, and Clinician Perspectives. *The Neurologist* 2017;22:207–214)
15. Penovich P, A Clinical Update on the Importance of Recognizing Seizure Clusters. https://www.medscape.org/viewarticle/863062
16. Ezeala-Adikaibe B A, Orjioke C, Ekenze O, Uchenna U, Onodugo O, Orakwue M et al. Prevalence of active convulsive epilepsy in an urban slum in Enugu South East Nigeria. Seizure 2016;35:100–105
17. Onwuekwe I O, Onodugo O D, Ezeala-Adikaibe B, Aguwa E N, Ejim E C, Ndukuba K et al. Pattern and presentation of epilepsy in Nigerian Africans: A study of trends in the southeast. *Trans R Soc Trop Med Hyg* 2009; 103(8):785-789.
18. Epilepsy: a public health imperative World Health Organization 2019. Last accessed
19. Dham BS, Hunter K, Rincon F. The epidemiology of status epilepticus in the United States. Neurocrit Care. 2014;20:476–83.
20. Amare, A.; Zenebe, G.; Hammack, J.; Davey, G. Status epilepticus: Clinical presentation, cause, outcome and predictors of death in 119 Ethiopian patients. Epilepsia 2008, 49, 600–607. [CrossRef] [PubMed]
21. Ong CT, Sheu SM, Tsai CF, Wong YS, Chen SC. Age-dependent sex difference of the incidence and mortality of status epilepticus: a twelve-year nationwide population-based cohort study in Taiwan. Plos one 2015;10(3):e0122350.
22. Sairanen JJ, Kantanen AM, Hyppölä HT, Kälviäinen RK. Treatment delay in status epilepticus – more effective pre hospital symptom recognition warranted. Scand J Trauma Resusc Emerg Med 2019;27(1):28.
23. Kantanen AM, Reinikainen M, Parviainen I, Kälviäinen R. Long-term outcome of refractory status epilepticus in adults: a retrospective population-based study. Epilepsy Res 2017;133:13–21.
24. Amare, A.; Zenebe, G.; Hammack, J.; Davey, G. Status epilepticus: Clinical presentation, cause, outcome and predictors of death in 119 Ethiopian patients. Epilepsia 2008, 49, 600–607. [CrossRef] [PubMed]
25. Neligan A, Shorvon S D,. Frequency and Prognosis of Convulsive Status Epilepticus of Different Causes A Systematic Review Arch Neurol. 2010;67(8):931-940
26. Jallon P, Zifkin B G. Seizure precipitants. In: Engels J jr, Pedley T A eds Epilepsy a Comprehensive Textbook. 2nd edition. Wolters Kluwer/Lippincott Williams and Wilkins. Health. Philadelphia 2008. Volume 1. Pp 77-80.
27. Sillanpää M, Schmidt D. Seizure clustering during drug treatment affects seizure outcome and mortality of childhood onset epilepsy. Brain. 2008;131:938-944.
28. Haut SR, Shinnar S, Moshé SL. Seizure clustering: risks and outcomes. Epilepsia. 2005;46:146-149.