Frequency of Nonconvulsive Seizures among Pediatric Systemic Cancer Patients with Acute Encephalopathy: Emergent Bedside EEG in Resource Constrained Communities

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Abstract: *Purpose:* To determine the incidence of nonconvulsive seizures (NCSz) among children with systemic cancer, who underwent unexplained acute severe encephalopathy (GCS≤8) during admission in ICUs and Neuro-ICUs.

Study Design: Multicenter prospective observational study describing sub-clinical seizures and electroencephalographic (EEG) features of children (1-16 years) with acute unexplained encephalopathy who underwent emergent bedside EEG≥30min monitoring.

Material and Methods: We conducted a prospective longitudinal observational study design and EEG assessment of 40 systemic cancer patients age ≤16years, consecutively diagnosed and admitted in intensive care units (ICUs) and neurointensive care units (Neuro-ICUs) of different cancer hospitals with unexplained acute impaired consciousness (GCS≤08) within ≤6hr of such deterioration. Bed-side EEG recordings of ≥30min were done according to the clinical scenario and the requirements of the treating neurologist/intensivist. Patients with brain tumor, brain metastasis, seizures or those with known cause of coma were excluded. Data surrounding clinical, electrographic, and treatment factors were collected *Via* a prospective systematic review of medical records and EEGs for correlation with diagnosis, change in the diagnosis and management.

Results: Over a period of 2 years, 40 children, 22.5% 1-5yeras, 37.5% 6-10years, 40% 11-16years; boys 65% and girls 35%, who had systemic cancer with a median age of 9.8 years with unexplained acute deterioration of conscious level (GCS≤08). This cohort underwent bed-side EEG of ≥30 min, which was abnormal in 100% of the records. The main reasons for EEG requests were: 1) unexplained impaired consciousness 22(55%) and 2) reason one plus subtle convulsion 18(45%). The most common EEG abnormalities were invariant mixed theta-delta slowing (27.5%), followed by Low-amplitude delta pattern plus epileptiform discharges (20%) and there was electrographic evidence of EEG seizures in 17(42.5%) of the cohort. These electrographic seizures were present in 55.5% of 18 patients with subtle convulsions, whereas were documented only in 20% of the 22 patients without such movements. Electrographic seizures among patients with subtle convulsions responded to antiseizure drugs in 75% cases as compared 50% such response among patients without such convulsions.

Conclusion: Emergent bed-side EEG record of ≥30 min is useful in systemic cancer patients admitted in NCUs and Neuro-ICUs with acutely impaired consciousness with or without abnormal body movements. Neurology consultation and EEG studies in these comatose patients provide useful diagnostic information.

Keywords: EEG, nonconvulsive seizures, encephalopathy, epileptiform discharges, neurointensive care units, systemic cancer.

1. INTRODUCTION

Systemic cancer pediatric patients are prone to become critically ill and are at high risk for a variety of neurologic insults, including seizures and encephalopathy, which can result in permanent neurologic disability if untreated 1. Despite these risks, there are few techniques for monitoring brain function during sudden deterioration of consciousness in these patients. An EEG measures the brain's electrical activity, monitors the dynamic functions of brain during recording time. The emergency electroencephalography (EEG), due to its low cost, the time required to carry out the examination, the lack of risk and personnel requirements, contributes greatly to the treatment of patients with acute diseases, in particular those with changes in consciousness 2,3. Irrespective of the underlying etiology, electrographic seizures (NCS) and electrographic status epilepticus (NCSE) are common in critically ill children and has been have been reported in 10–40% of critically ill children who undergo continuous electroencephalography (CEEG) monitoring in pediatric intensive care units (ICUs) or emergency departments 4,5. Electrographic seizures may be subdivided into electroclinical seizures (also referred to as convulsive seizures or clinically evident seizures) or nonconvulsive seizures (EEG-only seizures) 6. The most common use is for detection of non-convulsive seizures (NCS) and non-convulsive

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status epilepticus (NCSE) which are reported to occur in critically ill children 7, and information derived from EEG is reported to impact management in the majority of patients 8. To date, studies have not investigated detection and management of NCS in comatose systemic cancer pediatric patients and that NCS have been shown to affect processes that may lead to or worsen brain injury 9. Although urgent EEG studies in inpatients prompt changes in anticonvulsant management in 52% of adults 10, little data exist regarding optimal NCS management in admitted cancer pediatric patient with acute encephalopathy. We aimed to understand current clinical practice of emergent bedside EEG of ≥30 min, prevalence and management of NCS and NCSE among these patients admitted in critical care units.

2. METHODS

This is a prospective observational study of emergency EEGs obtained from systemic pediatric cancer patients from 1st January 2014 to 31st December 2016 submitted to urgent EEG examinations in intensive care units (ICUs) or in neurointensive care units (Neuro ICUs) of different cancer hospitals in Lahore, Pakistan. These entire urgent EEG requests were received at the Brain Associates, a neurophysiology laboratory located in center of this cosmopolitan city. The laboratory attends approximately 60 emergent EEG recordings per month.

2.1. Patient Identification

The patients with the diagnosis of systemic cancer who had unexplained sudden impaired consciousness (GCS≤08) of ≤06hr were assessed and an emergent bed-side EEG of ≥30min was monitored within ≤ 06hr of such clinical scenarios. We abstracted the clinical information written when the EEG was recorded and recorded the following parameters: etiology, age, sex, acuity of illness, clinical examination findings, presence of recent clinical seizures, and history of epilepsy. We reviewed the neuroimaging findings and recorded the presence or absence of brain space occupying lesion. The health records of study patients were reviewed on their bed side, discussed with on call resident, and inclusion determined based on the criteria below. Patients with abnormal movements but not definite convulsions due to seizures were included in the study cohort. Pre-treatment and follow up treatment plans after EEG reports with the treating neurologist/ intensives were reviewed.

2.2. Inclusion and Exclusion Criteria

Inclusion criteria consisted of: (1) age ≥1 year to 16 years, (2) diagnosis of Systemic cancer, 3) encephalopathy with GCS ≤08 of ≤06hr duration and (4) availability of EEG record and neuroimaging (CT or MRI) at the time of analysis. All neuroimaging features were ascertained from radiology reports, or when unclear, by review of neuroimaging films by the study neurologists. All of the original EEGs studies were personally reviewed by Dr. Malik and Dr. Choudhary. The acuity of the patient's disease relative to the timing of the EEG recording was classified as emergent ≤06 hr after documentation of deterioration of consciousness and these are admitted patients. Exclusion criteria consisted of: (1) Patients with brain tumor or brain metastasis, (2) diagnosis of epilepsy in past history, 3) status epilepticus preceding encephalopathy, 4) identifiable causes for encephalopathy were also excluded, 5) All patients who presented with generalized tonic-clonic SE or overt seizure activity were excluded and the patients who had seizures and/or were being treated with anti-seizure drugs and (6) patients with incomplete records and those in which EEG record was performed after ≥06hr of deterioration of the clinical condition.

3. DATA COLLECTION

3.1. Clinical Features

The records of the patients which contain their background characteristics such as age, sex, clinical, radiologic and pathological variables were analyzed. Pre-treatment and follow up treatment plan after EEG report and neurologist's consultation were reviewed. Clinical features assessed from medical records included: time of deterioration of consciousness and seizure/abnormal movements and their duration. Other clinical features included neurological examination and requirement for antiepileptic agents (single or multiple agents), however, EEGs were done before starting antiseizure drugs.

3.2. EEG Features

The emergency EEGs were performed by the laboratory of neurophysiology at the bedside in the corresponding health facility, majority were in Neuro-ICUs. EEGs were obtained in all of these patients within the first 06hr of making the diagnosis of coma and were obtained to evaluate the level of brain function and to evaluate overt seizure activity. Portable three EEG machines are available 24 hours with the laboratory. Electrodes were placed according to the

10/20 international system utilizing two Berg analogue apparatuses (time constant: 0.3; filter: 70 Hz; notch filter: 60 Hz; paper speed: 3 cm/second) with eight channels and two Nihon digital apparatuses (12-bit) with 22 channels. We maintained electrode impedance at less than 5 KΩ. We categorized EEG amplitudes into three bands: low (<100 μV), medium (100–300 μV) and 'high (>300μV) amplitudes. Background frequencies were grouped into three categories: delta, mixed theta and delta, and predominantly theta or greater frequency. We defined an EEG seizure as a distinct episode of epileptiform activity (sharp waves, spikes, sharp-slow waves, spike-slow waves and poly-spike-slow waves) over a minimum duration of 0.5sec, Only the first emergency proper EEG examination of each patient studied between 01/01/2014 and 31/12/2016 was included in this work, although some patients were submitted to as many as 10 examinations. The results were interpreted by two experienced neuro-physiologists (Malik and Choudhary) assisted by three EEG technologists, with the final decision being made by consensus. Electroencephalograms from previous sources and those with technically low quality examinations were excluded from the study. For study purposes, only the most significant alteration, whether related to the baseline rhythm or paroxistic disorders, was considered in each EEG; some examinations had more than one evident alteration. Thus, only one emergency EEG result was analyzed for each patient. The EEG background abnormalities were categorized into background type (normal or abnormal) and background asymmetry. The background activity was considered abnormal if the EEG demonstrated low voltage, discontinuity. The background asymmetry was defined as more than 50% difference in amplitude between each hemisphere. Lateralized EEG findings were defined as the presence of positive or negative sharp or slow waves originating from one hemisphere. The laterality of EEG features (right or left) was also recorded.

Patients were categorized as having NCSE only if 1) they fulfilled the criteria for SE, defined as continuous or nearly continuous electrographic seizure activity lasting at least 30 minutes without clinical seizure activity; and 2) at least two EEG interpreters independently agreed on the pattern represented seizure activity. The EEG criteria for NCSE consisted of discrete electrographic seizures, continuous spike and wave activity, or rhythmic recurrent epileptiform activity. Coma, coma nonconvulsive status epilepticus(coma –NCSE), coma-periodic discharges (lateralized periodic discharges (coma- LPDs) or coma with generalized periodic discharges (coma- GPDs), burst suppression patterns and evolution ictal EEG pattern were used according to Hirsch LJ, *et al*, [2].

4. RESULTS

4.1. Study Cohort

During the study period of 2years, 200 systemic cancer patients with acute medical coma (GCS≤8) within ≤06 hours were screened in this study. We excluded 160 patients, as study inclusion criteria were not met, primarily as ages were more than 16 years. All of these had emergent bedside EEG at least one record of ≥30min duration. Complete clinical information and neuroimaging findings were available on these 40(20% of the total study population children (≤16years of age-the study cohort), for 30(75%) of the 40 patients' short term follow- up information were available. Of the total 40 abnormal records, 22(55%) cases had coma without abnormal movements (no electrographic suspicion of seizures) and 18 (45%) cases had coma with possibility electrographic seizures. The mean age of the enrolled cohort was 10.5years (range 2 to 16years). Of the total boys were 26 (65%) and girls were 14(35%). The demographic characteristic and clinical presentation are shown in Table **1**.

Table 1: Characteristics of 40 Medically Comatose Pediatric Systemic Cancer Patients

No	Patient Characteristic	No. of Patients	Percentage
1	Boys	26	65
2	Girls	14	35
3	Age i. 1-5years	09	22.5
	ii. 1-5years	15	37.5
	iii. 11-16 years	16	40
4	Coma (GCS≤08).	22	55
5	Coma (GCS≤08) and abnormal movements	18	45

GCS- Glasgow Coma Scale.

4.2. EEG Findings

At least one bed-side EEG of ≥30 min was monitored on each these patients, which was abnormal with invariant to internal and external stimuli indicating encephalopathic EEG background in all of the records, and with asymmetry in 03(7.5%) of these records. Seventeen (42.5%) of the EEGs of patients in coma demonstrated predominant background of mixture of delta and theta waves but of age appropriate amplitude for EEG background, and a predominant low amplitude delta activities, invariant to internal and external stimuli, consistent with a electrographic diagnosis of severe encephalopathy were found in 18(45%) EEG records. Electro cerebral inactivity pattern (flat EEG-5%) was documented only among the group with no abnormal movements, whereas, theta and alpha coma were found in one case each, Table **2**.

We found 17 (42.5) patients in our EEG database had paroxysmal periodic discharges (GPDs) in addition to the severe encephalopathic EEG background. Among these total 17 (100%) EEGs, highest percentage of paroxysmal (epileptiform?) discharges were found in the records with features of Low-amplitude for age delta background (64.7%), as compared to paroxysmal (epileptiform?) discharges (35.3%) interspersed with mixed theta-delta age appropriate background, Table **3**.

Electrographic seizures were recorded in 07(31.8%) of the 22 patients without subtle convulsions, whereas electrographic seizures were in 10(55.5%) of the 18 such patients with abnormal movements in our study, which is statistically significant, Table **4**.

Table 2: Predominant EEG Patterns in Unexplained Acutely Comatose Systemic Cancer Pediatric Patients (n=40)

No	Predominant EEG Patterns	No. of Patients	Percentage
1	a. Invariant mixed theta-delta slowing	11	27.5
	b. Mixed theta-delta slowing plus epileptiform discharges	06	15
2	a. Invariant low-amplitude delta pattern	08	20
	b. Low-amplitude delta pattern plus epileptiform discharges	03	07.5
3	Continuous spike-wave discharges (NCSE) superadded to low amplitude delta background.	06	15
4	Intermittent burst- suppression pattern superadded to low amplitude delta background.	02	05
5	Electrocerebral inactivity pattern	02	05
6	Theta coma	01	02.5
7	Alpha coma	01	02.5
	Total	40	100

Table 3: Distribution of Different Electrographic Seizures among Comatose Systemic Cancer Pediatric Patients (n=17)

No	Electrographic Seizures' Pattern	No. of Patients	Percentage
1	Mixed theta-delta slowing interspersed with epileptiform discharges	06	35.3
2	Low-amplitude delta pattern interspersed epileptiform discharges	03	17.6
3	Low-amplitude delta interspersed with continuous spike-wave discharges (NCSE)	06	35.3
4	Low-amplitude delta with intermittent Burst- suppression pattern	02	11.8
	Total	17	100

Table 4: Prevalence of Electrographic Seizures among Comatose Children without and with Abnormal Movements (n=40)

No	Patient's Category	Electrographic Seizures	Percentage
1	Patients without abnormal movements (22)	07	31.8
2	Patients with abnormal movements (18)	10	55.5
	Total 40(100%)	17(42.5%)	

Table 5: Electrographic Seizures Response to Antiseizure Drugs among Comatose Children (n=14)

No	Patient's Category	Responsive to Antiseizure Drugs	Percentage
1	Electrographic seizures in patients with abnormal movements (08)	6	75
2	Electrographic seizures Patients without abnormal movements (06)	03	50
	Total 14(100)	09(64.3%)	

Follow-up EEG records 24-48 hours after intravenous anti- seizures medications (I/V AEDs) were available in 14(82.4%) of the 17 patients with possible electrographic seizures among comatose systemic cancer pediatric patients. Of these 14 patients, 09(64.3%) patients, EEG records after I/V AEDs showed improvement (electrographic seizures decreased ≥75%± clinical improvement) within 48 hours, usually after 24 hours, of the initial EEG records as recorded by the same set standards. The electrographic response to IV AEDs was documented among 50% and 75% of the patients without abnormal movements and with abnormal movements, respectively (statistically significant), Table **5**.

5. DISCUSSION

This multicenter prospective observational study demonstrates electrographic seizures (ES) and electrographic status epilepticus (ESE) among 40 children with systemic cancer undergoing bedside emergent ≥30min EEG, who had unexplained acute coma GCS≤8. Children with systemic cancer are at increased risk for life-threatening complications like sudden deterioration of consciousness or seizures either due to their malignancy or its treatment and sometimes no cause could be found for such complications 12. We documented male predominance (65%) with male: female ratio of 1.8:1. Our findings are in agreement with world literature as cancers that affect both males and females in all tissue systems frequently exhibit male:female incidence ratios that range from approximately 1.5:1–3:1 13-15.

Almost similar to our study, Jabeen *et al*. 16 reported that among 1250 pediatric cancer patients, the frequency of cancer was higher among boys (62%) than girls (38%) with a ratio of 1.6:1.

Age distribution analysis in our study population was different from the other international studies 17,18. We documented that 22.5% of the patients were younger than five years; 37.5%, were six to 10 years; 40% were 11 to 16 years of age. As compared to this Shochat *et al*. 17 showed that 32.5% of the patients were younger than six years; 15.5%, were six to 10 and 13.7% were 11 to 14 years. Whereas, Homes *et al*, 18 reported the highest percentage (n = 153, 32%) in their pediatric cancer patients of ≤4years of age. Most likely this difference is mainly due to the patient and clinical presentation selection bias, as ours was a very specialized pediatric population, admitted in hospitals and suffered from acute unexplained deterioration of unconsciousness.

Seizures in comatose children may manifest as overt convulsions, or subtle or electrographic seizures,19 but we excluded patients with overt convulsions. In a prospective study of 204 comatose children, over all seizures were observed in 54% before commencing EEG recording 20. Similarly we documented subtle seizures in 18(45%) and 22(55%) of the children were comatose without any clinical evidence of subtle seizures/abnormal movements. Almost the same percentage (23%) of clinically subtle seizures was documented in 82 children with acute non-traumatic coma 21.

EEG background was abnormal in all (100%) of all the patients with GCS≤ 8 in our study. This is in agreement with that various EEG patterns in coma correlate with the degree of impairment of consciousness and the depth of coma 22-24. So our study confirms that, the EEG reflects cerebral cortical activity, as modulated by brainstem and diencephalic inputs, so EEG abnormalities provide objective evidence for brain dysfunction. In 28 (70%) children, the background EEG activity was characterized by mixtures of theta-delta and low-amplitude delta activities, 6(15%) children had continuous spike-wave discharges (NCSE) superadded to delta background, intermittent burst-suppression pattern superadded to low amplitude delta background was documented in 2(5%) of the records. Electrocerebral inactivity pattern was obvious in 5%, whereas theta and alpha coma were in one patient each. Similarly, Gwer *et al*. 19 has reported in a prospective study of 92 acutely comatose children: 71 (87%) children, the initial background EEG activity was characterized by delta activity (<4 Hz) and only 11 (13%) had predominant frequencies of 4 Hz or

greater and 39 (48%) children had low background wave amplitude. These small variations are most likely due the different study cohorts. Electroclinical seizures refer to EEG seizures with a clinical correlate, whereas non convulsive seizures refer to seizures without any clinical correlate identified by bedside caregivers or video review by encephalographers [23, 24]. Internationally studies have documented electrographic seizures in 7–65% of comatose children [25-28]. One of the lowest percentage (7%) of electroclinical seizures has been reported from Australia25, which included children only with GCS<8, the same GCS as in our cohort. In this study, all epileptic seizures were documented in first 3 hours of video –EEG monitoring, pointing the importance of initial EEG record. Majority of these studies have included children of different age groups, varied etiology including, conditions that are not primarily neurological, like our study population, but none studied pediatric systemic cancer patients as our study cohort. We documented electrographic seizures in 45% and electrographic status epilepticus occurred in 15% of our cohort. In comparison, Claassen *et al*. [29] in a retrospective study of 570 hospitalized patients documented electrographic seizures in 19% but seizures were most frequent in younger patients (36% of children under age 18 had seizures). Overall in our mixed cohort of 200 adults and children we found electrographic seizures in 41%, but different finding was that 55.5% of the children with subtle convulsions had electrographic seizures, whereas, these were found only in 31.8% of the children with no subtle convulsions. Almost similar to our results, in a prospective study of 100 critically ill children, electrographic seizures are reported in 46% and electrographic status epilepticus in 19% 30. Of interest, all these studies, including ours, indicate that although there are significant differences in the acute neurologic categories (epilepsy-related, acute structural, acute nonstructural) monitored across institutions, within each acute neurologic diagnosis category there hardly any significant difference in electrographic seizure occurrence. In agreement with our study in a single center observational study of children with acute encephalopathy undergoing continuous EEG demonstrated that ES occurred in 21% (41/200) and ESE occurred in 22% (43/200)31. Most electrographic seizures in critically ill children are nonconvulsive seizures 31, but in our prospective study of 40 children, electrographic seizures only were recorded in 42.5% of the children who had previous neurological disorders.

Importantly, neither electrographic seizures nor electrographic status epilepticus are 100% clinical seizures 32. Patients experiencing some seizures with a clinical correlate might be identified by close observation, while patients with exclusively electrographic-only seizures cannot be identified without EEG monitoring. To validate this, we analyzed the dataset for the patients whose follow-up bedside EEG≥ 30min were available after 24-48hr of I/V AEDs. Data was available on 14 patients, of these 9 (64.3%) patients showed significant electrographic ± clinical response. In comparison in a study of 200 children, ES terminated after administration of the first AED in 74% of children while ESE terminated after administration of the first AED in only 21% of children 23. We observed the maximum response in children with subtle convulsions (75%) as compared with children with no convulsions (50%). These data demonstrate that 42.5% of the children with systemic cancer who present with acute unexplained encephalopathy have evidence of electrographic seizures, and of these about 64% have electro-clinical seizures.

This observational study has limitations. First, this was a single disease cohort, which limits generalizability for different etiologies causing encephalopathy in children. Second, this was a snap shot EEG study, whereas continuous or video EEG monitoring are superior to snap shot EEG of ≥30min. Thirdly different centers may have different treatment practices regarding the speed of seizure identification, overall management approach, and specific AED choices. Treatment delays have been associated with lower response rates in children with convulsive status epilepticus [34, 35]. Clinical Descriptions may have underestimated the frequency of convulsive activity, and outcome data were incomplete.

CONCLUSION

These data suggest that for management for acute encephalopathy in children with systemic cancer is very important and snap shot ≥30min bedside EEG is very useful where video or continuous EEG recording is not available. Further prospective studies are needed to establish whether electrographic seizures are an epiphenomenon and simply reflect brain injury or whether they cause neuronal injury and worsen outcome.

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CONTRIBUTORS

All authors contributed equally in the design and conduct of the study.

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COMPETING INTERESTS

None.

ETHICS APPROVAL

This study was approved by the ethical committee of the Brain Associates.

PROVENANCE AND PEER REVIEW

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REFERENCES

[1] Zeman A. Consciousness Brain 2001; 124: 1263-1289.

[2] Kaplan PW. The EEG in metabolic encephalopathy and coma. J Clin Neurophysiol 2004; 21: 307-318.4. 3. Husain AM. Electroencephalographic assessment of coma. J Clin Neurophysiol 2006; 23: 208-220

[3] Shahwan A, Bailey C, Shekerdemian L and Harvey AS. The prevalence of seizures in comatose children in the pediatric intensive care unit: a prospective video-EEG study. Epilepsia 2010; 51: 1198-1204. https://doi.org/10.1111/j.1528-1167.2009.02517.x

[4] Kirkham FJ, Wade AM, Mcelduff F, Boyd SG, Tasker RC, *et al*. Seizures in 204 comatose children: incidence and outcome. Intensive Care Med 2012; 38: 853-862. https://doi.org/10.1007/s00134-012-2529-9

[5] Abend NS, Dlugos DJ, Hahn CD, Hirsch LJ and Herman ST. Use of EEG monitoring and management of non-convulsive seizures in critically ill patients: a survey of neurologists. Neurocrit Care 2010; 12: 382-389. https://doi.org/10.1007/s12028-010-9337-2

[6] Jette N, Claassen J, Emerson RG and Hirsch LJ. Frequency and predictors of nonconvulsive seizures during continuous electroencephalographic monitoring in critically ill children. Arch Neurol 2006; 63: 1750-5. https://doi.org/10.1001/archneur.63.12.1750

[7] Vespa PM, Nenov V and Nuwer MR. Continuous EEG monitoring in the intensive care unit: early findings and clinical efficacy. J Clin Neurophysiol 1999; 16: 1-13. https://doi.org/10.1097/00004691-199901000-00001

[8] Vespa PM, Miller C, McArthur D, *et al*. Nonconvulsive electrographic seizures after traumatic brain injury result in a delayed, prolonged increase in intracranial pressure and metabolic crisis. Crit Care Med 2007; 35: 2830-6. https://doi.org/10.1097/00003246-200712000-00023

[9] Kilbride RD, Costello DJ and Chiappa KH. How seizure detection by continuous electroencephalographic monitoring affects the prescribing of antiepileptic medications. Arch Neurol 2009; 66: 723-8. https://doi.org/10.1001/archneurol.2009.100

[10] Hirsch LJ, LaRoche SM, Gaspard N, Gerard E, Svoronos A, *et al*. American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 version. J Clin Neurophysiol 2013; 30(1): 1-27. https://doi.org/10.1097/WNP.0b013e3182784729

[11] Pan IJ, Daniels JL and Zhu K. Poverty and childhood cancer incidence in the United States. Cancer Causes Control 2010; 21: 1139-1145. https://doi.org/10.1007/s10552-010-9528-3

[12] ParkinDM, WhelanSL, FerlayJ, TeppoL, ThomasDB, eds. Cancer incidence in five continents, Lyon. International Agency for Research on Cancer. IARC Scientific Publication 2002; 8: 155.

[13] American Cancer Society:(http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-044552.pdf)

[14] The Cancer Research UK. http://www.cancerresearchuk.org/cancer info/cancerstats/incidence/).

[15] Jabeen S, Haque M, Islam MJ, *et al*. Profile of pediatric malignancies five years study. Dhaka Med Coll 2010; 19(1): 33-38.

[16] Shochat JS, Fremgen MA, Sharon B, Murphy BS, *et al*. Childhood Cancer: Patterns of Protocol Participation in a National Survey. CA Cancer J Clin 2001; 51: 119-130 https://doi.org/10.3322/canjclin.51.2.119

[17] Homes LJr, Vandenberg J, McClarin L, *et al*. Epidemiologic, Racial and Healthographic Mapping of Delaware Pediatric Cancer: 2004-2014. Int J Environ Res Public Health 2016; 13(49): 1-14.

[18] Gwer S, Idro R, Fegan G. *et al*. Continuous EEG monitoring in Kenyan children with non-traumatic coma. Intensive Care Med 2012; 38(5): 853-862. https://doi.org/10.1136/archdischild-2011-300935

[19] Fenella J, Kirkham JF, Wade MA and McElduff F. Seizures in 204 comatose children: incidence and outcome. Intensive Care Med 2012; 38(5): 853-862. https://doi.org/10.1007/s00134-012-2529-9

[20] Crawley J, Smith S, Muthinji P, *et al*. Electroencephalographic and clinical features of cerebral malaria. Arch Dis Child 2001; 84: 247-53. https://doi.org/10.1136/adc.84.3.247

[21] Trinka EHJ. EEG in coma and brain death. Klin Neurophysiol 2011; 42(3): 141-8. https://doi.org/10.1055/s-0031-1276898

[22] Bauer G, Trinka E and Kaplan PW. EEG patterns in hypoxic encephalopathies (postcardiac arrest syndrome): fluctuations, transitions, and reactions. J Clin Neurophysiol 2013; 30(5): 477-89. https://doi.org/10.1097/WNP.0b013e3182a73e47

[23] Abend NS, Chapman KE, Gallentine WB, Goldstein J, Hyslop AE, *et al*. Electroencephalographic monitoring in the pediatric intensive care unit. Curr Neurol Neurosci Rep 2013; 13: 330. https://doi.org/10.1007/s11910-012-0330-3

[24] Tsuchida TN, Wusthoff CJ, Shellhaas RA, *et al*. American Clinical Neurophysiology Society Standardized EEG Terminology and Categorization for the Description of Continuous EEG Monitoring in Neonates: report of the American Clinical Neurophysiology Society Critical Care Monitoring Committee. J Clin Neurophysiol 2013; 30: 161-173. https://doi.org/10.1097/WNP.0b013e3182872b24

[25] Shahwan A, Bailey C, Shekerdemian L, *et al*. The prevalence of seizures in comatose children in the pediatric intensive care unit: a prospective video-EEG study. Epilepsia 2010; 51: 1198-204. https://doi.org/10.1111/j.1528-1167.2009.02517.x

[26] Tay SK, Hirsch LJ, Leary L, *et al*. Nonconvulsive status epilepticus in children: clinical and EEG characteristics. Epilepsia 2006; 47: 1504-9. https://doi.org/10.1111/j.1528-1167.2006.00623.x

[27] Abend NS and Dlugos DJ. Nonconvulsive status epilepticus in a pediatric intensive care unit. Pediatr Neurol 2007; 37: 165-70. https://doi.org/10.1016/j.pediatrneurol.2007.05.012

[28] Saengpattrachai M, Sharma R, Hunjan A, *et al*. Nonconvulsive seizures in the pediatric intensive care unit: etiology, EEG, and brain imaging findings. Epilepsia 2006; 47: 1510-18. https://doi.org/10.1111/j.1528-1167.2006.00624.x

[29] Claassen J, Mayer AS, Kowalski GR, *et al*. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. NEUROLOGY 2004; 62: 1743-1748. https://doi.org/10.1212/01.WNL.0000125184.88797.62

[30] Abend SN, Gutierrez-Colina MA, Topjian AA, *et al*. Nonconvulsive seizures are common in critically ill children. Neurology 2011; 76(12): 1071-1077. https://doi.org/10.1212/WNL.0b013e318211c19e

[31] Kirkham FJ, Wade AM, Mcelduff F, Boyd SG, Tasker RC, *et al*. Seizures in 204 comatose children: incidence and outcome. Intensive Care Med 2012; 38: 853-862. https://doi.org/10.1007/s00134-012-2529-9

[32] Nicholas S. Abend MD, I Sarah M Sanchez BS and 1 Robert A Berg MD. Current Treatment of Electrographic Seizures and Status Epilepticus in Critically Ill Children: a Single Center Experience. Seizure 2013; 22(6): 467-471. https://doi.org/10.1016/j.seizure.2013.03.008

[33] Fernández SI, Abend SN, Arndt HD, *et al*. Electrographic seizures after convulsive status epilepticus in children and young adults. A retrospective multicenter study. J Pediatr 2014; 164(2): 339-346.e2. https://doi.org/10.1016/j.jpeds.2013.09.032

[34] Eriksson K, Metsaranta P, Huhtala H, Auvinen A, Kuusela AL, *et al*. Treatment delay and the risk of prolonged status epilepticus. Neurology 2005; 65: 1316-8. https://doi.org/10.1212/01.wnl.0000180959.31355.92

[35] Lewena S and Young S. When benzodiazepines fail: how effective is second line therapy for status epilepticus in children? Emergency Medicine Australasia 2006; 18: 45-50. https://doi.org/10.1111/j.1742-6723.2006.00807.x

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