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Correlating Clinical Features with EEG findings and Neuroimaging (MRI) abnormalities in Children with Seizure disorder

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Abstract
BACKGROUND*: Seizure disorder is one of the most common treatable neurological disorders of brain.The essential diagnostic evaluation for unprovoked seizure remains source of debate. Only few studies have evaluated the utility of EEG (Electroencephalogram) and Neuroimaging in seizure disorder in clinical practice.*
OBJECTIVE*: To determine correlation between clinical features, EEG findings and neuroimaging (MRI-Magnetic Resonance Imaging) abnormalities in children with seizure disorder.*
MATERIAL AND METHODS: *It is cross sectional, non-interventional, observational study carried out from March 2014 to May 2015. We enrolled children diagnosed with seizure disorder, following in pediatric outpatient department as well as patients admitted in pediatric wards.*
RESULT*: Predominant etiology of seizure disorder was structural/metabolic (59%) andgenetic (39%) children. Sixty six had abnormal EEG with Generalized epileptiform discharges (35) ,focal epileptiform discharges (29) and hypsarrhythmia (2). Abnormal neuroimaging found in 59%. Commonest neuroimaging abnormality was ring enhancing lesion (19%). Statistically significant correlation found between delayed development, neurocutaneous marker, number of convulsions and type of therapy with the abnormalities in EEG. Statistically significant association found between neonatal convulsion, abnormal birth history, microcephaly and etiology of seizure with Neuroimaging abnormality.*
CONCLUSION: *We found high frequency of imaging abnormalities in children with new-onset seizures who were otherwise developing normally. Our findings indicate that EEG results are not good indicators of MRI results and they should not be used as the only criterion for ordering MRI.*
Keywords*: EEG, MRI, Seizure disorder*

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I. Introduction

Seizure disorder is one of the most common treatable neurological disorders of the Brain[1].Seizure disorder is a general term that is usually used to include any one of several disorders including epilepsy, febrile seizures, and possibly single seizures and seizures secondary to metabolic, infectious or other etiologies .Epilepsy is disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological, and social consequences of this condition [2]. Approximately 30% of patients who have first afebrile seizure have later epilepsy; the risk is approximately 20% if neurologic exam, EEG, and neuroimaging are normal [2]. The essential diagnostic evaluation for an unprovoked seizure remains a source of debate.

EEG andNeuroimaging are two usual ways to use for this propose. Thegoal of the diagnostic assessment is to prepare evidence that helps establish ordisprove the diagnosis of epilepsy and to determine thecause of epilepsy to classify the epileptic syndrome. EEG helps determine seizure type and epilepsy syndrome, and thereby choice of antiepileptic medication and prediction of prognosis. EEG findings contribute in terms of whether the seizure disorder is focal or generalised, idiopathic or symptomatic, or part of aspecific epilepsy syndrome.

Imaging is recommended when localization-related epilepsy is known or suspected, when the epilepsy classification is in doubt, or when an epilepsy syndrome with remote symptomatic cause is suspected. The basic role of radiological imaging in epilepsy is to define any structural anomalies or pathologies and to aid in the patient treatment protocol.MRI is considered the imaging modality of choice because of superior anatomic resolution and characterization ofpathologic processes, versatility, and lack of radiation .The sensitivity of MRI in identifying epileptogenic foci in patients with medically refractory patients has been reported to be more than 80% [3].

II. Material And Methods

It is a cross sectional, non-interventional, observational study carried out from March 2014 to May 2015.Children between 1 month to 18 years diagnosed with seizure disorder, following up in pediatric outpatient department as well asadmitted in the pediatric wards and satisfying the inclusion criteria were enrolled.A written informed consent of the parents and assent of the subject (if over 7 years of age) were obtained prior to participation.Ethical committee approval was taken.

Inclusion Criteria:

1. Children aged between one month and eighteen years.

Exclusion Criteria:

1) Neonatal seizures (less than 1 month): Neonates were excluded as they have various possible etiologies for seizures.

2) Parents /Patients who refused to consent for inclusion in the study.

Asurface EEG was performed for all of the patients andany abnormalities were annotated. The
EEG was only interpreted via single pediatricNeurologist. All children undergoing MRI of the brain and EEG details of the findings was recorded in the proforma .The neuroimaging in our study included MRI Brain (using seimensmagnetom maestro class, 1.5 Tesla) done as per Epilepsy Protocol. The films were reported independently by radiologist who has extensive epilepsy imaging experience.

ILAE 2010 recommendations was used to classify seizure type and etiology. Treatment outcome was classified as remission (no seizures without drug treatment), conditional remission (no seizures under treatment) and treatment resistance (seizures even on 2 or more appropriate anti epileptic drugs)[4].

Data Analysis

Association between qualitative variables was assessed by Chi-Square test, with Continuity Correction for all 2 X 2 tables and by Fisher's exact test for all 2 X 2 tables where Chi-Square test was not valid due to small counts. Quantitative data was represented using Mean ± SD and Median & IQR (Interquartile range). Analysis of Quantitative data between Qualitative variable with two subgroups was done using unpaired t-test if the data passed 'Normality test' or by Mann-Whitney Test if data failed 'Normality test'. Appropriate statistical software, including but not restricted to MS Excel, PSPP was used for statistical analysis.

III. Results

Total of 100 children diagnosed with seizure disorder were enrolled.We attempted to determine the correlation of various clinical characteristics namely gender, age of onset, seizure type, history of neonatal convulsions, family history of epilepsy, birth history, developmental history, head circumference, neurocutaneous markers, frequency of convulsions, focal neurological deficits, neurological examination, etiology of seizure, type of therapy received, outcome with EEG findings and neuroimaging (MRI) findings.

The study population ranged from two and half months to seventeen years with a mean age of 7.31 years (SD =3.738) and median of 8 years. Male to female ratio was 1.3. Only 6% of the children had positive family history.About 13% of the children had abnormal birth history, 14% children had delayed developmental milestones in one or more domains and the correlation with EEG abnormality was statistically significant with p value =0.031.66% of children had abnormal EEG. Generalized epileptiform discharges were found in 35% of children while 29 % had focal epileptiform discharges. 2 children had EEG suggestive of hypsarrhythmia. The age of onset of epilepsy ranged from 1 month to 11.6 years with mean age of onset of epilepsy of 4.626 year (SD = 3.32). Forty two children had generalized seizure and 43 had focal seizure. The predominant etiology of epilepsy was structural/metabolic (59%) whereas genetic epilepsy was seen in 39% children.The outcome in our study was grouped as Remission (no seizures without treatment), Conditional remission (no seizures under treatment) and Treatment Resistance (seizures on 2 or more anti-epileptic drugs) (4). At the time of enrollment, 15% children had achieved remission, 63% children were under conditional remission (74.5% on monotherapy and 25.5% on polytherapy) .22% children were refractory to treatment even on polytherapy and the correlation with EEG abnormality was significant(p value=0.037).Various neurocutaneous markers observed were Hypomelanotic macule, Café au lait spot, Ash leaf spot and shagreen patch. 85.7% children withneurocutaneous markers had EEG abnormalities and the correlation was statistically significant (p=0.033).There was no significant correlation found between abnormal EEG and age of onset of seizures, history of neonatal seizures, positive family history,abnormal birth history,microcephaly,neurocutaneous markers,type of seizure,outcome and abnormal neuroimaging findings.

Abnormal neuroimaging was found in 59% of the children. Out of them 51 had at least one MRI abnormality and two or more abnormalities were identified in 8 children. Most common MRI abnormality observed was ring enhancing lesion (19%). Of these, 12 children had Neurocysticercosis and 7 children with Tuberculomas.Other MRI abnormalities found were atrophy & gliosis, pachygyria, polymicrogyria, periventricular leucomalacia, encephalomalacia, choroidal cyst.

MRI abnormality was seen in all children with structural/metabolic (symptomatic)which the association was meaningful (p value = 1.20E-22).Abnormal MRI findings were seen in all children with history of neonatal convulsion and 54.9% without this history which the difference was meaningful(p=0.010).There are significant differences between abnormal birth history and MRI abnormalities against the patients with normal birth history (p=0.003) .MRI abnormality was found in all children with microcephaly and 53.9% without microcephaly which the difference was meaningful (p=0.002).MRI abnormality was found in 63.3% of children with abnormal EEG and 50 % of children wihout this finding and the difference was insignificant(p=0.272).
There was no significant correlation found between abnormal neuroimaging and age of onset of seizures, positive family history,developmental delay, neurocutaneous markers,type of seizure,type of therapy and outcome.

IV. Discussion

Childhood seizures occur most commonly in 1-24 months with a decreasing incidence throughout the remainder of childhood [5] [6]. Seizures may occur in up to 10% of population, whereas epilepsy is a chronic disease characterized by recurrent seizures which affects 2% of the population[5]. In almost all studies it was noticed that there is a slight male predominance [7].The practice parameter for a first afebrile seizure developed by the Quality Standards Subcommittee of the American Academy of Neurology, Child Neurology Society, and American Epilepsy Society recommends EEG as a standard part of diagnostic investigation. The EEG is necessary to determine the epilepsy syndrome and the diagnosis of an epilepsy syndrome may be helpful in determining the need for imaging studies. The EEG is also useful in predicting the prognosis for recurrences. An urgent neuroimaging for children with postictal focal neurologic deficits (Todd's paresis) not quickly resolving, or who has not returned to baseline within several hours after the seizure. Strong consideration is recommended for non-urgent neuroimaging in certain clinical circumstances, including cognitive or motor impairment of uncertain etiology, unexplained abnormalities on neurologic examination, abnormal EEGs not representing a benign syndrome, seizures of partial onset, or in children under the age of 1 year [8] [9]. National Institute of Health and Clinical Excellence (NICE) guidelines recommend that all patients with epilepsy should be imaged with magnetic resonance imaging [(10)]. The ILAE Subcommittee for Pediatric Neuroimaging has proposed guidelines for imaging infants and children with recent-onset epilepsy Indications for Structural Neuroimaging [11].

In the present study, we have tried to determine the relation between clinical features of seizure disorder, EEG & abnormalities on neuroimaging (MRI) with respect to etiology, therapy (treatment) and outcome.

EEG abnormality was found in 57.8 % children on monotherapy while 80.6 % on polytherapy. The correlation was significant (p value=0.037). The results were comparable to study conducted by Sinha s et al, showed that presence of epileptiform activity predict the use of polytherapy (p = 0.004, odds ratio = 3.3) [12].
Abnormal neuroimaging was found in 59% of the children that is more than other previous studies.This difference could be abnormal MRI findings hadsignificant relation with etiology of seizure,history of neonatal seizures ,abnormal birth history and microcephaly.

Positive family history as adverse prognostic factor was not found in our study as only 6% of the children had positive family history in first degree relatives. This needs to be interpreted with caution as epilepsy in the family is considered a stigma in Indian social conditions .So the history may not be forthcoming.
Most common neuroimaging abnormality observed in our study was ring enhancing lesion (19%). Probably, the very high prevalence and incidence of neuro-infections particularly Neurocysticercosis and Tuberculosis being the most common parasitic infection of the central nervous system in developing countries is the reason for such large number of ring enhancing lesions being observed in our study. The results of neuroimaging abnormality in our study were comparable with various other studies. In a study done by U C Wieshmann, they found an abnormal neuroimaging in 51% of patients. The most commonly detected abnormality in their study was hippocampal sclerosis, followed by non-specific abnormalities, vascular abnormalities, tumors, brain damage and malformations of cortical development[13]. In another study by Sanjib Sinha et al. neuroimaging abnormality found was around 53% [14].

MRI abnormality was seen in all children with structural/ metabolic (symptomatic) which the association meaningful (p value = 1.20E-22).Anna T Berg et al. found in their multiple logistic regression analysis of all imaged patients, the type of epilepsy (idiopathic versus non-idiopathic) non-idiopathic epilepsy and abnormal motor-sensory (neurological) examinations as predictors of a positive MRI scan [15].
Abnormal neuroimaging was found in 63.6% children with abnormal EEG and 50% without this and the difference was not significant(p=0.272). These finding suggests that normal EEG did not reliably predict a normal MRI and normal results on EEG should not be used to place a patient in a low-risk group that does not need an MRI for a complete evaluation.The results were consistent with study done by Doescher JS et al (p value=0.0954) [16] .

There were few limitations to our study. There may be referral biases as our study was conducted at an urban tertiary referral center. Our data are also dependent upon parental and witness recollection. Sample size was small. Younger patients or infants with more severe seizures (frequent, prolonged and generalized) are more likely to be evaluated urgently in an emergency department rather than an outpatient office. The decision to obtain MRI was based upon clinical judgment. Being a tertiary referral pediatric Centre , the patients likely reflect the more severe end of spectrum of children with seizures and milder cases are likely to be under presented. Children presenting to primary physician with single seizure or with unrecognized seizures may be missed due to non-referral.

V. Conclusion

We found high frequency of imaging abnormalities in children with new-onset seizures who were otherwise developing normally. This study shows that EEG results are not good indicators of MRI results and they should not be used as the only criterion for ordering MRI.

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