Magnetic Resonance Imaging Brain in Evaluation of Pediatric Epilepsy

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Abstract

Introduction: About 5% children are at risk of experiencing a seizure and half of them encounter the first seizure in infancy. Epilepsy is a condition in which seizures are triggered recurrently from within. Electroencephalograph and neurosonogram are often the initial diagnostic workup for seizure activity. They have the benefits of being non-invasive and avoiding radiation exposure. Computed tomography is helpful in detection of calcific foci; however, it has the risk of radiation exposure. Magnetic resonance imaging (MRI) is the imaging modality of choice due to its ability to depict neuroanatomy, excellent gray white matter differentiation, status of myelination and detection of focal structural brain lesions.

Purpose: The aim of study was to detect and characterize various lesions causing epilepsy in pediatric age group (0–12 years) and also to detect frequency with which they occurred using MRI.

Methods: The study was performed on 95 children under the age of 12 years over a period of 2 years who presented with epilepsy. Patients with trauma and febrile seizure disorders were excluded. Conventional and contrast MRI was performed in all cases and lesions were characterized in location, signal intensity, and other features.

Results: The mean age group of the study population was 4 years 3 months. Generalized seizures constituted the major seizure group being present in 66.3%. Our study shows infection (29.8%) as the most common etiology followed by anoxia and hypoxic-ischemic encephalopathy. Mesial temporal sclerosis (57.1%) was the most common pathology seen in isolated temporal lobe epilepsy. Demyelinating diseases and neoplasm constituted 3.6% patients each.

Conclusion: MRI is the imaging modality of choice in the evaluation of pediatric patients presenting with epilepsy. Proper MRI seizure protocol helps to establish the correct diagnosis, plan the management according to diagnosis as well as helps in prognosis.

Key words: Brain, Epilepsy, Magnetic resonance imaging, Pediatric

INTRODUCTION

A seizure is defined as a sudden, paroxysmal electrical discharge from the central nervous system (CNS) resulting in involuntary motor, sensory or autonomic disturbances with or without alteration in sensorium. The age and neurodevelopmental maturity status determine the clinical manifestation and type of seizure disorder. About 5% children are at risk of experiencing a seizure and half of them encounter the first seizure in infancy. Prevalence is greater in the neonatal period (almost 1% in term and 20% in preterm). In infancy, febrile convulsions are the most frequent form. Epilepsy is a condition in which seizures are triggered recurrently from within. It is considered to be present when two or more unprovoked seizures occur at an interval >24 h apart. The cumulative lifetime incidence of epilepsy is 3%, and more than half the cases begin in childhood. The annual prevalence of epilepsy is lower (0.5–0.8%) because many children outgrow epilepsy. Children with epilepsy should undergo neuroimaging if one or more of the following indications are present:

a. If there is any evidence to suggest that epilepsy is localization-related (e.g. focal), with the exception of typical benign idiopathic partial epilepsy. The basis
for establishing localization-related seizures includes the characteristics of the seizure, abnormalities on an electroencephalograph (EEG), focal examination (including Todd's paralysis), and history or examination to suggest remote symptomatic cause (such as extreme prematurity, meningitis, encephalitis, complicated febrile convulsion, or significant head injury).

b. Abnormal neurologic examination including focal deficits, stigmata of neurocutaneous, cerebral malformation syndrome, or a history of significant developmental delay, arrest, or regression.

c. Children younger than 2 years, excluding those with simple febrile seizures.

d. Children with characteristics of a symptomatic generalized epilepsy syndrome, including infantile spasms or early Lennox-Gastaut syndrome.

e. Failure to control seizures, worsening seizures, changes in seizure manifestations, or developmental regressions also merit neuroimaging if not previously performed.

f. Finally, new-onset seizures/epilepsy presenting with evidence for a medical emergency such as increased intracranial pressure or status epilepticus always merit emergency imaging.\[3\]

The EEG is helpful when it is clearly abnormal but 40–50% of patients with epilepsy have a normal single interictal EEG. On the other hand, about 5% of non-epileptic patients may have non-specific EEG abnormalities. Despite its limitations, the EEG is a simple non-invasive and relatively inexpensive test that gives useful information if used judiciously and correlated with the clinical description of seizures. When abnormal, it is helpful in making a correct diagnosis of epilepsy and may even help in the choice of anti-epileptic drug therapy in a given case. Ultrasound is often the initial study in a diagnostic workup for seizure activity. It has the benefits of being non-invasive and avoiding radiation exposure. Neonatal head ultrasound's primary role has traditionally been in the evaluation of the preterm newborn for diagnosis of parenchymal hemorrhage, germinal matrix hemorrhage, and hydrocephalus. Ultrasound may detect changes of hypoxic-ischemic injury, vascular anomalies, or brain malformations.\[4\] Computed tomography (CT) is helpful in the identification of intracranial hemorrhage, major vascular malformations, and ventriculomegaly. The sensitivity of CT is approximately 30% in the detection of many of the causes of epilepsy. Given these limitations, as well as the risks of radiation exposure in infants and young children, CT has been replaced by magnetic resonance imaging (MRI) in the elective workup of childhood epilepsy.\[4\] MRI is the imaging modality of choice due to its ability to depict neuroanatomy, excellent gray white matter differentiation, status of myelination and detection of focal structural brain lesions.\[2\] MRI is the technique of choice to identify underlying cause in partial seizures. Even when enhanced MRI has been compared with contrast enhanced CT; the superiority of MRI is seen especially in temporal lobe origin, since lesions in inferior temporal lobes may be inapparent on CT scan due to beam hardening artifacts. The accuracy of cranial MRI diagnosis has been improved by the introduction of paramagnetic contrast agent gadopentetate dimeglumine. It increases the detection rate of certain intracranial lesions especially those of vascular nature and those involving the meninges. It significantly improves radiologic specificity particularly with regard to defining the extent or nature of certain neoplasms and the differentiation of aggressive from benign processes. Coregistration of MRI with other functional imaging modalities such as positron emission tomography and single-photon emission CT have also been proven valuable in localization of structural and functional alteration.\[5\] The role of MRI in epilepsy surgery in identifying the epileptogenic focus also lies in its ability to depict topographic relationships between epileptogenic lesion and the eloquent regions of the brain.\[5\] Post-operative MRI may detect causes of failure such as inadequate resection and can monitor tumor recurrence on follow-up imaging.\[5\] MRI is especially useful for prognosticating post-operative seizure control. This study proposes to evaluate the role of MRI in detection and characterization of causes and their frequency for pediatric epilepsy and to assess its diagnostic utility.

Aims and Objectives

To detect and characterize the lesions causing epilepsy in pediatric age group (0–12 years) and to detect the frequency of etiological factors responsible for epilepsy using MRI.

MATERIAL AND METHODS

A hospital based prospective time bound clinical study was carried out in a Tertiary Care Centre over a duration of 2 years. The sample size was 95. All pediatric patients (age under 12 years) referred from outpatient department and inpatient department who presented with epilepsy were included. Patients with metallic implants, claustrophobia, trauma, and febrile seizure disorders were excluded. All patients were subjected to MRI using Philips Achieva 1.5 Tesla machine. Conventional MRI was performed by taking T1W (TE 8.0 ms, TR 480 ms), T2W (TE 102.9 ms, TR 4780 ms), and fluid-attenuated inversion recovery (FLAIR) (TE 92.2 ms, TR 8002 ms) sequences. Post-gadolinium (dose 0.1 mmol/kg) enhanced MRI was performed in axial and sagittal planes in selected cases depending on findings on non-contrast study or clinical suspicion. Diffusion-weighted imaging (TE 83 ms, TR 5025 ms) and gradient recalled echo axial performed in all cases. When required,
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MR spectroscopy, venous 3-dimensional phase contrast angiography and MR angiography including time of flight were done. MRI was assessed for any possible neurological causative lesion of seizures. Lesions were characterized in location, signal intensity and other features seen on different MRI sequences. Statistical analysis - data were collected and entered into MS Excel. Statistical calculations were made, and results of this study were analyzed and compared with other available studies in literature. Findings of EEG and CT scan if done were documented and correlated with imaging findings. Final diagnosis was based on the medical history, clinical presentation, EEG and CT correlation, follow-up cerebrospinal fluid analysis, pathological, surgical findings when available and response to medical therapy. In inconclusive cases, it was made by follow-up MRI and treatment response. Ethical clearance was obtained from the Ethical Committee of the Institution for this study.

RESULTS

Out of 95 patients, 63 patients (66.3%) presented with generalized seizures, 21 patients (22.1%) presented with focal seizures while 11 patients (11.6%) had an unknown onset. 84 patients (88.4%) had positive findings on MRI while 11 patients (11.6%) had normal MRI with no detectable lesions. Most of the patients in the study were in the age group of 0–3 years followed by 10–12 years. There was a male preponderance with male:female ratio of 2.1:1. Infection comprised 25 patients (29.8%), followed by anoxia and hypoxic-ischemic encephalopathy (HIE) in 21 patients (25.0%). Malformations of cortical development (MCD) were seen next in 12 patients (14.3%). Phakomatoses and vascular causes constituted 5 patients each (5.9%). Mesial temporal sclerosis (MTS) and miscellaneous causes constituted 4 patients each (4.8%). Demyelinating diseases and neoplasm were seen in 3 patients each (3.6%). Least common were inherited metabolic disorders comprising 2 patients (2.4%). Thus, most common etiology in our study was infection comprising 25 patients (29.8%) followed by anoxia, hypoxic-ischemic encephalopathy in 21 patients (25.0%).

Most common etiology in our study was infection comprising 25 patients (29.8%) followed by anoxia, hypoxic-ischemic encephalopathy in 21 patients (25.0%). Malformations of cortical development (MCD) were seen next in 12 patients (14.3%). Phakomatoses and vascular causes constituted 5 patients each (5.9%). Mesial temporal sclerosis (MTS) and miscellaneous causes constituted 4 patients each (4.8%). Demyelinating diseases and neoplasm were seen in 3 patients each (3.6%). Least common were inherited metabolic disorders comprising 2 patients (2.4%). Thus, most common etiology in our study was infection followed by anoxia and HIE [Figure 1]. Only temporal lobe was affected in 7 patients causing isolated temporal lobe epilepsy. Out of them, MTS was most frequently seen in 4 patients (57.1%). Focal cortical dysplasia (FCD), dysembryoplastic neuroepithelial tumors (DNET), and tuberculosis (TB) with tuberculomas constituted the remainder with 1 patients each (14.3%). All 4 patients of MTS showed the presence of hippocampal atrophy and secondary changes (temporal horn dilatation). Loss of hippocampal architecture was present in 3 patients (75%) and hippocampal T2, FLAIR hyperintensity was present in 2 patients (50%) [Figure 2]. MCD constituted 12 patients presenting with epilepsy. Out of them, FCD [Figure 3] was seen in 4 patients (33.3%). Corpus callosal dysgenesis/agenesis (CCD/CCA) and polymicrogyria constituted 3 patients (25.0%) each. Pachygyria constituted 2 patients (16.5%) while microcephaly with simplified gyral pattern, heterotopia, hemimegalencephaly (HMEG), and holoprosencephaly (HP) (lobar) constituted the remainder
with 1 patient (8.3%) each. Four patients had multiple pathologies. One had pachygyria with HMEG. Other 3 patients had pachygyria with polymicrogyria, CCD/CCA with HP (lobar), and FCD with polymicrogyria, respectively. Out of 5 patients with phakomatoses, 3 patients (60.0%) had tuberous sclerosis (TS). Sturge-Weber syndrome (SWS) and neurofibromatosis 1 (NF1) were seen in 1 patient (20.0%) each [Figure 4]. Out of 2 patients with inherited metabolic disorders, MELAS and metachromatic leukodystrophy constituted 1 patient (50%) each. Anoxia and HIE were the cause of epilepsy in 21 patients in our study. Out of them, 12 patients (57.2%) and 9 patients (42.8%) were preterm and term, respectively, based on the clinical information elicited [Figure 5]. Among the neuroimaging findings, leukomalacia was the most common finding seen in 11 patients (52.4%) followed by cystic changes seen in 8 patients (38.0%). White matter volume loss was next common seen in 7 patients (33.3%), and intracranial hemorrhage was seen only in 1 patient (4.7%). In our study, the cause of seizures in 25 patients was infectious etiology. TB was seen in 7 patients (28.0%), neurocysticercosis in 6 patients (24.0%), encephalitis in 5 patients (20.0%), meningoencephalitis in 3 patients (12.0%), and pyogenic abscess in 2 patients (8.0%). Meningitis (excluding tuberculous), Subdural empyema, and Rasmussen’s encephalitis constituted 1 patient (4.0%) each. One patient had both meningoencephalitis with pyogenic abscess. Thus, in our study, most common pathology in patients with infectious etiology was TB followed by neurocysticercosis [Figures 6 and 7]. Out of 7 patients found to have TB, 5 patients (71.4%) had tuberculomas. 4 patients (57.1%) demonstrated leptomeningeal enhancement and 2 patients (28.6%) had infarcts. 1 patient (14.3%) had tuberculous abscess. Communicating hydrocephalus was associated only in 1 patient (14.3%). None of the patient showed cranial nerve involvement (CNI). Neoplasm comprised 3 patients in our study. DNET, hypothalamic hamartoma, and choroid plexus papilloma were seen in 1 patient (33.3%) each [Figure 8]. Vascular etiology was responsible for seizures in 5 patients. 3 (60.0%) of them had arterial infarcts (excluding tuberculous), 1 (20.0%) had arteriovenous malformation while another patient (20.0%) had cavernous angiomia with a developmental venous anomaly [Figure 9]. None of the patient had venous infarct. Four patients were grouped under miscellaneous causes with postictal edema, aqueductal stenosis, arachnoid cyst, and idiopathic intracranial hypertension seen in 1 patient (25.0%) each.

**DISCUSSION**

In our study of total 95 patients, maximum (57.9%) were in the age group of 0–3 years. The mean age group of the study population was 4 years 3 months. Our study is in discordance with the study conducted by Gulati et al. in which maximum patients were in the age group 6–12 years. It is also in discordance with the study conducted by Wongladarom et al. in which mean age group of the study population was 7 years and 5 months. Male:female ratio in our study was 2.1:1 and correlates with the study conducted by Sanghvi et al. in which 60.5% were males and 31.7% were females. Studies conducted by Gulati et al., Amirsalari et al., and Zajac et al. also showed similar findings in which males outnumber females. Generalized seizures constituted the major seizure group being present in as many as 66.3% in our study and correlate with the study conducted by Chaurasia et al. in which it was seen in 76.7% patients. 84 patients (88.4%)
had abnormal MRI findings in our study. Kuzniecky et al. found MRI abnormalities in 84% of patients.\textsuperscript{12} Our study is comparable with the studies of Chaurasia et al., Gulati et al., Kumar et al. and shows infection as the most common etiology in pediatric epilepsy.\textsuperscript{11,13,14} This may be due to a higher prevalence of infection in developing countries like India. Infectious etiology was seen in 25 patients in which most common was TB found in 7 patients (28.0%), followed by neurocysticercosis in 6 patients (24%), encephalitis in 5 patients (20.0%), meningocoelephalitis in 3 patients (12.0%), pyogenic abscess in 2 patients (8.0%), subdural empyema in 1 patient (4.0%), and Rasmussen's encephalitis in 1 patient (4.0%). In Gulati et al. study, out of 158 patients with structural abnormalities on MRI, tuberculoma was the most common lesion present in 40% followed by neurocysticercosis in 17%.\textsuperscript{6} In a study by Chaurasia et al., the most common cause of epilepsy was CNS TB (30.3%), followed by neurocysticercosis (11.0%) and encephalitis (7.9%).\textsuperscript{11} Our study thus correlates with the above-mentioned studies. However, our study is in discordance with Kumar et al. study, in which most common etiology was neurocysticercosis (55.81%) followed by tuberculoma (29.91%).\textsuperscript{14} 7 out of 84 patients (8.3%) had isolated temporal lobe involvement. MTS was most commonly seen in 57.1% of them. Our study correlates with study conducted by Grattan-Smith et al. in which MTS was seen in 30 out of 53 children (57%) of patients with temporal lobe epilepsy.\textsuperscript{15} All 4 patients with MTS in our study showed
hippocampal atrophy and secondary change (dilatation of temporal horn). Loss of hippocampal architecture was seen in 75% and hippocampal T2, FLAIR hyperintensity in 50% of patients. Our study is in discordance with Ng et al., in which out of 24 patients with MTS, hippocampal T2 hyperintensity was seen in 20 patients (83.3%), hippocampal atrophy in 19 patients (79.2%), loss of hippocampal architecture in 13 patients (54.2%), and secondary change (decreased hippocampal T1-weighted signal) in 3 patients (12.5%). There are significant differences as regards to the most frequent pathology in MCD in various studies published in literature. In our study, among out of 12 patients having MCD, FCD was the most common in 4 patients (33.3%). Our study correlates with study conducted by Mittal et al., in which out of 54 patients with MCD, FCD was the most common seen in 16 patients (29.6%).

Our study does not correlate with study conducted by Sadek et al., in which out of 50 patients with MCD, lissencephaly was most commonly found in 42% and FCD was seen in only 10% cases. Another study conducted by Güngör et al., who studied 101 patients with MCD, found polymicrogyria to be the most common in 53.4%. Out of 5 patients of phakomatoses, 3 (60.0%) had TS, SWS was seen in 1 (20.0%), and NF1 (20.0%). Our study does not correlate with a study conducted by Dietrich et al., in which neuroimaging study of 29 patients with medically intractable seizures was done. The study included other studies than MRI for neuroimaging and neurophakomatoses was the etiology in 5 (17.4%) patients. In the study, most common phakomatoses was SWS seen in 3 patients (60.0%), TS in 1 (20.0%), and NF1 (20.0%). Our study is in discordance with study conducted by Güngör et al., in which out of 5 patients having MCD, FCD was the most common seen in 16 patients (29.6%).

In our study, only 2 patients had imaging findings of inherited metabolic disorders with MELAS seen in 1 patient (50.0%) and metachromatic leukodystrophy in another (50.0%) patient. No comparable data were available as to the most frequent pathology in inherited metabolic disorders causing pediatric epilepsy. In our study, anoxia and HIE were seen in 21 patients. 12 patients (57.2%) were preterm and 9 patients (42.8%) were term. Among the neuroimaging findings, most common was leukomalacia was seen in 11 patients (52.4%), followed by cystic changes in 8 patients (38.0%), white matter volume loss in 7 patients (33.3%), and intracranial hemorrhage in 1 patient (4.7%). Our study does not correlate with study conducted by Alam and Sahu, in which 45 children with history of perinatal asphyxia were studied. Most common pathology was arteriovenous malformation found in 12 patients (92.3%) in age group >10–18 years had arteriovenous malformation, and the remaining 1 patient (20%) had bilateral carotid occlusion. Our study also does not correlate with the study conducted by Wongladarom et al., in which vascular disorder was responsible for epilepsy in 5 patients (5%). Out of them, 2 patients (40%) had moyamoya disease, 1 patient (20%) had cavernous angioma, 1 patient (20%) had arteriogenous malformation, and the remaining 1 patient (20%) had bilateral carotid occlusion. Our study also does not correlate with Pilarska and Lema study, in which out of 20 patients with cerebrovascular anomalies, the most common pathology was arteriogenous malformation found in 13 patients (65%). For etiology in age group 0–3 years, our study correlates well with Khreisat study, in which children suffering from epilepsy below the age of 2 years were studied. The most common etiological factor found in this study was perinatal asphyxia seen in 55%, followed by CNS infection in 15%, anomalies of CNS in (9%), head injuries in (8%), congenital and heredofamilial disorders in (8%), and prematurity in (5%). For etiology in older age group, our study correlates with Kumar et al. study, in which children in the age group of 28 days to 18 years with partial seizures were studied.

6 patients (66.6%) in age group of 28 days – 5 years, 18 patients (85.7%) in age group of >5–10 years and 12 patients (92.3%) in age group >10–18 years had infection as the most common etiology. Thus infection had major burden in causing epilepsy with increasing age group. For etiology in older age group, our study also correlates with Gulati, et al. study, in which 170 children with chronic seizures were studied. Age distribution was done as follows: 0–1 year, 1–3 year, 3–6 year, and 6–12 year. The etiologies were classified into infections (tuberculomas, neurocysticercosis, and meningitis), atrophy, vascular, and miscellaneous causes. Infection was most common etiology in 6–12 years age group seen in 51.1%, followed by miscellaneous in 16.4%. In age group 0–1, 1–3, and 3–6 years, infection was seen in 4.7%, 4.1%, and 3%, respectively. This study had 4 patients with abnormal MRI grouped under miscellaneous cause. Postictal edema was seen in 1 patient (25.0%), aqueductal stenosis in 1 patient (25.0%), arachnoid cyst in 1 patient (25.0%), and idiopathic intracranial hypertension in 1 patient (25.0%). We found
3 patients showing imaging findings of demyelination in our study. One of them showed typical imaging findings of acute disseminated encephalomyelitis in 1 patient (33.3%). MRI findings of patchy hyperintense signal in bilateral corona radiate and centrum semiovale on T2W and FLAIR images, showing restricted diffusion with nodular enhancement on post-contrast T1W images was seen in 1 patient each (33.3%). No comparable studies were available as some of the published studies which we have gone through had discussed the above etiologies under a single heading. This study emphasizes the revolution brought about by MRI in evaluating pediatric epilepsies. The results of our study as regards to sex distribution, most common type of epilepsy and its correlation with MRI, distribution according to type of etiology, pathologies causing isolated temporal lobe epilepsy, neuroimaging findings in TB, distribution according to pathologies in MCD, infection, neoplasm and distribution according to various etiologies and age group are comparable with previous published studies in literature. However, the results are discordance with previous studies regarding age distribution, neuroimaging findings in MTS, anoxia and HIE, distribution according to pathologies in MCD, phakomatoses, and vascular cause. We could not find any comparable data mentioning the most frequent pathology in inherited metabolic disorders, demyelination and among miscellaneous causes.

CONCLUSION

In the evaluation of pediatric patients with seizure disorder, it is important to arrive at an accurate diagnosis of cause of seizure for treatment decision. With its high spatial resolution, excellent inherent soft tissue contrast, multiplanar imaging capability and lack of ionizing radiation, and MRI have emerged as a versatile tool in imaging of pediatric patients with seizures. Employing appropriate imaging protocols and reviewing the images in systemic manner helps in the identification of subtle epileptogenic structural abnormalities. MRI could be the first investigation of choice in epileptic syndrome, developmental cortical malformations, and MTS. Its ability in identifying subtle lesions, location, and extent of the lesions is excellent. Hence, we conclude that MRI plays a significant role in the evaluation of pediatric patients presenting with epilepsy and it is the first imaging modality of choice with proper MRI seizure protocol to establish the correct diagnosis, plan the management according to diagnosis as well as helps in prognosis.

REFERENCES