

# The role of magnetic resonance imaging brain in estimating the burden of preventable and potentially curable epilepsy in developmentally normal children”

Jaya Upadhyay, Prachi Chaudhary, S Thora

From Department of Pediatrics, M.G.M. Medical College, Indore, Madhya Pradesh, India

**Correspondence to:** Dr. Prachi Chaudhary, A -504, Sky Heights Apartment, B. Road, Near Navlakha Square, Indore – 452 001, Madhya Pradesh, India. Phone: +91-9826043219. E-mail: drprachi.ch@gmail.com

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## ABSTRACT

**Background:** Epilepsy is the most common neurological condition among children. Diagnosis of epilepsy is clinical, but to find the etiology we must depend on investigations such as electroencephalography (EEG) and magnetic resonance imaging (MRI) of the brain. EEG is more useful to diagnose genetic epilepsies, and MRI is more useful in structural causes. **Objective:** The objective of this study was to find the etiology of epilepsy prevalent in children of our region and to evaluate the role MRI brain in diagnosis. **Methods:** This was a survey-based study conducted at a tertiary care hospital in central India, between April 2015 and August 2016. A total of 108 developmentally normal children in the age group of 1 month to 14 years who presented with two or more unprovoked seizures 24 h apart or known case of epilepsy and on treatment admitted in the inpatient department for seizures were included in this study. The patients were classified based on detailed history, personal observation of seizures in some cases, thorough clinical examination, EEG recording, MRI findings, and other relevant investigations pertaining to the case, and the data were analyzed. **Results:** According to the ILAE 2010 classification, 12.9% of our patients had probable genetic epilepsy, 32.4% belonged to the structural metabolic group, and 54%, the largest proportion had an unknown cause. Of total 42 patients with abnormal MRI, 30 (71.42%) patient had underlying structural or metabolic abnormality, whereas 28.57% had a genetic cause. 10 patients had imaging results suggestive of neurocysticercosis, while 7 patients had mesial temporal sclerosis. Gliosis was seen in nine patients, tuberculoma was seen in four patients, and finding suggestive of infarcts was seen in six patients. Remaining patients had abnormalities including corpus callosal agenesis (1), cortical dysplasia (2), tuberous sclerosis (1), white matter disease (1), and hippocampal hyperintensities suggestive of encephalitis (1). **Conclusion:** MRI brain is the most important routinely available investigation and must be utilized. Neurocysticercosis is still the most common structural cause of epilepsy in children in our region.

**Key words:** *preventable epilepsy, epilepsy protocol MRI, epilepsy burden*

Epilepsy is a chronic neurological disorder that affects individuals of all ages from birth to senescence. According to the definition proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE), Epilepsy is defined as a condition characterised by recurrent (two or more) epileptic seizures unprovoked by any immediate identified cause [1]. The incidence of epilepsy is approximately 0.3 to 0.5%, and the prevalence is approximately estimated to be five to ten persons per 1000. It is estimated in various studies that the overall prevalence of epilepsy in India is 5.59–10 per 1000 populations with no gender or geographical difference [2]. The most widely used classification of epileptic seizures is the ILAE classification, which is principally based on the clinical seizure type and interictal electroencephalography (EEG) findings.

No good data were found to identify the incidence of various etiologies of the condition in India. In this study, we have tried to identify the cause of epilepsy in developmentally normal

children presented to our institute over the period of 1 year to get some understanding of the situation and specially to find out the proportion of cases, which are potentially preventable or curable.

## MATERIALS AND METHODS

This is a prospective observational study, which included 108 children in the age group of 1 month to 14 years who were presented to our institute between April 2015 and August 2016 with two or more unprovoked seizures 24 h apart or an already known case of epilepsy and on treatment admitted in inpatient department. The institute is one of the biggest tertiary level referral centers of central MP and has a widespread drainage area of patient inflow, especially the neurology patients. It caters mainly to the lower and middle socioeconomic strata of society.

Patients with cerebral palsy, global developmental delay, post-encephalitis sequelae, and other obvious causes of symptomatic

epilepsy due to gross brain damage were excluded from the study. Only the children who otherwise had normal development were included in the study. Simple Trivandrum Development Screening Test was used to screen for developmental delay. A detailed medical history, including family history and birth history, was taken and also detailed history related to seizures and physical examination was done in all the patients. The patients who had a significant birth history but had development in the normal range on the Trivandrum Screening test were included in the study. All cases were classified according to the proposed diagnostic scheme for people with epilepsy, ILAE Task Force on Classification and Terminology, 2010 for epileptic seizures.

A 16-channel EEG recording was obtained from all the patients using various activation procedures. Recordings were reported by a neurologist. Magnetic resonance imaging was done using AVANTO 8 CHANNEL, 1.5 TESLA equipment from Siemens. All the patients underwent MRI brain by dedicated Epilepsy Protocol as per ILAE 1997 guidelines for neuroimaging in epilepsy consisting of the following sequences: T2 axial fast spin echo; fluid-attenuated inversion recovery sequence – axial, diffusion-weighted sequence, T1 IR sequence – axial; T1 IR coronal oblique – 3 mm slices; T2 coronal oblique – 3 mm slices; T1 spoiled gradient-recalled echo – sagittal (three dimension magnetization prepared rapid gradient echo [MPRAGE]). The MRI brain in most patients was done at our institute. If a patient had a previously done imaging, which fulfilled our requirements done on at least 1.5 Tesla machine, and all the required sections were taken according to epilepsy, it was also accepted and reviewed by our radiologist. Other practically possible investigations were also done to find out the etiology of epilepsy.

The predominant seizure type was defined as the most frequent type of seizure occurring in the previous 6 months in patients with more than one seizure type. The patients were classified based on detailed history, personal observation of seizures in some cases, thorough clinical examination, EEG recording, MRI findings, and other relevant investigations pertaining to the case. The relative frequencies of various types of seizures in our patients were studied. Sex distribution, age of onset of seizures, clinical correlation, and the probable etiology of the epilepsy were analyzed, and the patients were classified accordingly.

This was a survey-based study, and the results have been presented as a percentage.

## RESULTS

A total of 150 children were considered for inclusion of which 28 were excluded as 12 had cerebral palsy, 3 had neurodegenerative disease, 5 had post-encephalitic sequelae, 6 had West syndrome, and 2 had other epilepsy syndromes. Of the remaining 122 patients, 4 did not give consent and 10 could not get the imaging or EEG done, leaving 108 patients who were included in the study.

The 54% of patients were female and 46% were male. They belonged to the age group of 1 month to 14 years. Maximum patients (47.5%) had the onset of seizures in the age

group of 1–5 years. 5.5% had onset at <1 year of age, 26.8% between 5 and 10 years, and 20% above 10 of age. The most common seizure type observed in the study population was generalized (64.8%) – as shown in Table 1.

According to the ILAE 2010 classification, 12.9% of our patients had probable genetic epilepsy, 32.4% belonged to the structural metabolic group, and 54%, the largest proportion had an unknown cause. In this study, all 108 patients underwent MRI brain by epilepsy protocol. Of 108 patients, 38.89% (42) had abnormalities in MRI (Table 2).

57.14% of patients with focal seizures had an abnormal MRI, whereas 27.69% of patients with generalized seizures had abnormal MRI. In this study, out of total, 42 patients had abnormal MRI, 30 (71.42%) patients had underlying structural or metabolic abnormality, whereas 28.57% had a genetic cause. This emphasizes the importance of MRI as a diagnostic tool.

Of the 42 cases where the neuroimaging was abnormal, the following findings were noted. The most common MRI abnormality detected in this study group is neurocysticercosis followed by gliosis and mesial temporal sclerosis. A total of 10 patients had imaging results suggestive of neurocysticercosis, while 7 patients had mesial temporal sclerosis, which is intractable epilepsy amenable to surgery. Gliosis was seen in nine patients, tuberculoma was seen in four patients, finding suggestive of infarcts was seen in six patients. Remaining patients had abnormalities including corpus callosal agenesis (1), cortical dysplasia (2), tuberous sclerosis (1), white matter disease (1), and hippocampal hyperintensities suggestive of encephalitis (1).

## DISCUSSION

Childhood epilepsy is the most important cause of neurological morbidity in children worldwide. There is not enough published literature from the region of central India. Our hospital is one of the biggest referral centers in the region of central MP, especially for neurological patients, and so the distribution of etiology in this group gives an idea of the burden in the general pediatric population.

This prospective observational study was planned to find out the proportion of potentially curable causes of childhood epilepsy in developmentally normal children. The grossly neurologically impaired children due to an obvious cause were excluded from the study. Exclusion of this group decreases the number of structural (remote symptomatic) etiology. 108 patients who were developmentally normal and between 1 month and 14 years of age group who were presented with new onset two or more unprovoked seizures 24 h apart or known case of epilepsy were included in the study.

When classified according to ILAE 2010 classification [3], 12.9% of our patients had probable genetic epilepsy, 32.4% belonged to the structural metabolic group, and 54%, the largest proportion had an unknown cause. Shah *et al* reported 30.8% of symptomatic epilepsy [4], 41% by Cavazutti *et al.* [5], and 22%–53% patients in a study done by Mac *et al.* [6] had symptomatic epilepsy, which is now known as structural. In a study done in

Hyderabad in 1998 by Murthy *et al.* [7], of 2531 cases, 48% fell into cryptogenic (unknown), without unequivocal generalized or focal seizures. Most studies from India report low numbers of idiopathic genetic syndromes due to lack of diagnostic facilities.

12.96% of total 108 patients had some probable genetic component that included hippocampal atrophy or sclerosis with no acquired etiology, 4 children had a very strong family history of epilepsy in siblings with the same pattern of epilepsy, and EEG had abnormal discharges and normal neuroimaging. 54.62% (59) patients had unknown etiology, which included patients not meeting the criteria of genetic or structural epilepsy. We had excluded the patients with global developmental delay and known genetic syndromes, so these proportions are not a true reflection of etiology in the population, rather these were the findings in the overtly neurologically normal children. The very high proportion of the group with unknown cause may be because of either these patient selection criteria or unavailability of detailed genetic analysis.

However, the structural metabolic group was well diagnosed due to the better availability of imaging facilities. In this study, out of total 42 patients with abnormal MRI, 71.42% patient had underlying structural or metabolic abnormality, whereas 28.57% has a genetic cause. Focal seizures are more commonly associated with abnormal neuroimaging as compared to generalized seizures. A study conducted by Mcbee *et al.* [8] on neuroimaging with first-onset seizures observed that the frequency of abnormal neuroimaging was higher in focal seizures than generalized seizures in neurologically normal children. Similarly, Bachman *et al.* [9] also found abnormal MRI results in 38.89% patients.

Of our 108 patients, 32.48% (34) patients had underlying structural cause of seizure, which included CNS granulomas such as neurocysticercosis (10), tuberculoma (4), gliosis and periventricular leukomalacia suggestive of old hypoxic-ischemic insult (9), infarction, which included both old and recent infarction (6), cortical dysplasia (2), corpus callosal agenesis (1), white matter changes (1), and hippocampal hyperintensities (1). Out of these, neurocysticercosis, tuberculomas, and birth injury were the causes that are preventable. As only children with normal development were included in the study, the majority of children with severe birth injury were already excluded from the study. Hence, these birth injuries found on neuroimaging did not cause any major developmental delay and neurological impairment but presented with seizures. This implies that 22.2% (24/108) of developmentally normal children with epilepsy were suffering from causes that can be prevented. Improving hygienic conditions, improving the education and awareness among people, and providing better healthcare facilities can decrease the incidence of these conditions.

The results were similar to many other studies done in India. Various studies from India have shown neurocysticercosis as the most common identifiable etiology of seizures. Neurocysticercosis accounted for 47% of all identifiable etiologies in the CRESSstudy [10]. Murthy *et al.* have shown 51% of new-onset partial epilepsy is due to calcified or non-calcified neurocysticercosis [7]. Rajasekharhas reported 34% of patients with active epilepsy diagnosed with NCC [11]. Their

**Table 1: Distribution of seizure types in study group**

| S.no. | Type of seizure | Number of cases (%) (n=108) |
|-------|-----------------|-----------------------------|
| 1     | Generalized     | 70 (64.81)                  |
| 1a    | Tonic-clonic    | 53 (75.71)                  |
| 1b    | Tonic           | 14 (20)                     |
| 1c    | Myoclonic       | 02 (2.85)                   |
| 1d    | Atonic          | 01 (1.43)                   |
| 2     | Focal           | 38 (35.18)                  |

**Table 2: Distribution of MRI imaging findings**

| Imaging finding              | Number of cases (n=42) (%) |
|------------------------------|----------------------------|
| Infarcts                     | 6 (14.28)                  |
| NCC                          | 10 (23.80)                 |
| Corpus callosal agenesis     | 1 (2.38)                   |
| Gliosis                      | 9 (21.43)                  |
| Cortical dysplasia           | 2 (4.76)                   |
| Mesial temporal sclerosis    | 7 (16.66)                  |
| Tuberculoma                  | 4 (9.52)                   |
| Tuberous sclerosis           | 1 (2.38)                   |
| White matter changes         | 1 (2.38)                   |
| Hippocampal hyperintensities | 1 (2.38)                   |

MRI: Magnetic resonance imaging, NCC: Neurocysticercosis

study included door-to-door survey of 50,617 people between 2 and 60 years in urban and rural settings. They found NCC to be equally prevalent in pediatric and adult population and also in rural and urban settings. NCC incidence has state-wise differences too, the incidence being very high in Delhi and surrounding areas and very low in Kerela [12]. However, overall in studies from all the regions, NCC has remained the topmost cause of structural epilepsies over the last two to three decades.

EEG has a role to play in the diagnosis of epilepsy syndromes. Of 108 patients, 38 patients had normal EEG and normal MRI, while EEG abnormalities were present in 62 patients, and MRI abnormalities were detected in 42 patients.

This study shows a significant correlation between the findings of EEG and MRI brain. From our study, we found that MRI along with clinical history and EEG should be used in the initial assessment of patients with epilepsy. The most common etiology for epilepsy in developing country like India is neurocysticercosis, and hence, neuroimaging is a mandatory consideration. Furthermore, in patients with focal and, in particular, medial temporal lobe pathology, there is a chance of successful surgical treatment. Thus, MRI brain adds to improvement in diagnosis and treatment possibilities in patients with epilepsy.

This was a single-center study, and the drainage population was not defined; hence, the prevalence calculation was not possible. Furthermore, there are a large number of patients with unknown etiology. This might be because we did not get MRI on 3.0 Tesla machine, which could have better picked up conditions like neuronal migration disorders. There was a limited use of genetic tests and other sophisticated investigations such as video EEG monitoring, mainly due to the cost considerations, which makes definitive diagnosis difficult in most situations.

## CONCLUSION

Even after excluding patients with obvious symptomatic epilepsy, a good number of patients were found to have structural epilepsy, a significant proportion of which is preventable and amenable to treatment. NCC is still the most common cause of structural epilepsy. Sincere efforts should be made at the community level to control preventable diseases such as NCC, TB, and birth injuries.

Presently, MRI brain is the most important and easily available tool in the evaluation of patients with epilepsy, and it must be utilized to the maximum. Even in poor patients, the findings of exact etiology are very helpful in providing proper care and management. Considering the high incidence of structural epilepsy, it is cost effective to get a good MRI brain done in all patients, especially those who are developmentally normal.

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