ECRONICON OPEN ACCESS

EC NEUROLOGY
Research Article

Pattern of Epilepsy in a Paediatric Neurology Clinic of a Tertiary Care Hospital in Eastern India with Special Reference to Etiology, Seizure Semiology, Diagnosis and Treatment Gap

Sreeparna Dey[1], Manoj Kumar Mahata[2]*, Saikat Ghosh[3], Sarbajit Das[3], Ramesh Bhattacharya[4], KC Ghosh[4] and GP Mondal[5]

[1]*Postgraduate Trainee, Department of Gynaecology, IPGME&R, Kolkata, India*

[2]*Associate Consultant, Department of Neurology and Neurointervention, Woodlands Multispeciality Hospital Limited, Kolkata, India*

[3]*Senior Resident, Department of Neurology, Calcutta National Medical College, Kolkata, India*

[4]*Associate Professor, Department of Neurology, Calcutta National Medical College, Kolkata, India*

[5]*Professor and HOD, Department of Neurology, Calcutta National Medical College, Kolkata, India*

***Corresponding Author:** Manoj Kumar Mahata, Associate Consultant, Dept of Neurology and Neurointervention, Woodlands Multispeciality Hospital Limited, Kolkata, India.

Received: April 03, 2019; **Published:** May 27, 2019

Abstract

Background: Epilepsies are common childhood morbidities worldwide and they are associated with significant socio-cultural, economic and health implications in the developing countries. Although, it is readily diagnosed clinically from the history of recurrent afebrile seizures, the classification of the disorder which facilitates appropriate therapy may be difficult in the resource poor parts of the developing country where neurodiagnostic facilities may not be readily available.

Objective: Our purposes are to identify the exact type of epilepsy and its etiology, to formulate the appropriate therapy, to assess treatment response and to find out the causes for treatment gap.

Methods: Systemic random sampling of patients attending pediatric neurology clinic, designed as observational study involving clinical and diagnostic evaluation and follow up.

Results: Our study empathetically establishes the contribution perinatal hypoxic ischemic injuries as an important cause of the early childhood onset epilepsies. Treatment gap in epilepsy includes cost of therapy, lack of parental education, use of alternative of medicines and social stigma.

Keywords: *Childhood Epilepsy; Perinatal Brain Injury; Seizure Semiology; Treatment Gap*

Abbreviations

AED: Anti Epileptic Drug; EEG: Electroencephalography; PEC: Perinatal Encephaloclastic HIE: Hypoxic Ischemic Encephalopathy; PVL: Periventricular Leukomalacia; NHBI: Neonatal Hypoglycemic Brain Injury; CPS-T: Complex Partial Seizure: Temporal; CPS-ET: Complex Partial Seizure: Extratemporal; LSCS: Lower Segment Caesarian Section; IED: Interictal Discharge

Introduction

Epilepsy affects nearly 50 million people worldwide without any national, geographical, ethnical, age and sex boundaries. The disease burden of epilepsy is 1 percent and it causes 6.4 million disability-adjusted life years (DALYs) worldwide and it causes 1.32 million years

of life (YLL) loss [1]. Almost 80 percent people with epilepsy living in developing country including India. Almost 6 to 10 million people are suffering from epilepsy in India [2]. Epilepsy is one of cost intensive disorder. It causes huge burden to the individuals, health care providers and society at large [3]. The first year of human life is associated with the highest incidence of epilepsy [4]. During infancy a unique interface exists between epilepsy and normal brain maturation [5]. The causes of remote symptomatic seizure, occurring in early childhood are different from adults, it also differs in developing countries like India comparing to developed countries [5]. Newborn distress, developmental delay, head trauma and family history are the risk factors associated with epilepsy, which account for 40% of the risk of epilepsy in children. Maternal factors like consanguineous marriage, age of the mother at delivery, recurrent abortions, antenatal infections, gestational hypertension, gestational diabetes were not associated with development of epilepsy. Newborn distress was associated with early onset of epilepsy [6]. Possible determinants of treatment gap in their study: health care resources, cultural believes, treatment seeking behaviour, antiepileptic drug (AED) prescription pattern by the medical community, reasons for poor drug adherence, and purchasing capacity [7].

Materials and Methods

This is an observational study, based on systemic random sampling involving clinical and diagnostic evaluation and at least one follow up after initiation of treatment. Maximum of our patients were undergone at least monthly follow up. All patient of epilepsy attending pediatric neurology clinic at Calcutta National Medical College and Hospital, which is a tertiary care hospital situated in the city of Kolkata in eastern part of India, were screened. 117 infants and children below 12 yrs of age, fulfilling the definition of epilepsy or with history of first episode of unprovoked seizure (if EEG suggestive of epileptic syndrome) were included within February 2016 to September 2017.

Patients with non-epileptic events (both psychogenic and physiologic) or first episode of unprovoked seizure (if EEG does not suggest any epileptic syndrome) were excluded from the study.

The study proposal has been approved by the Ethical Committee of the institution prior to the commencement of the study. During the study ethical issues were dealt rigorously according to revised Helsinki 2000 protocol.

The diagnosis of epilepsy requires the occurrence of at least 1 unprovoked epileptic seizure with either a second such seizure or [5] enough electroencephalography (EEG) and clinical information to demonstrate an enduring predisposition to develop recurrences of seizures. For epidemiological purposes, the diagnosis of epilepsy is made when 2 or more unprovoked epileptic seizures in a time frame of more than 24 hours [8-10].

Statistical data analysis

After collecting all the data, a grand chart was prepared using Microsoft Office Excel 2007 and statistical analysis was performed using SPSS -20 statistical software for analysis of data. Mean and standard deviation (SD) were calculated separately. P-value of < 0.05 was taken as significant.

Observation and Results

Demographic profile

In our study, lowest age of the patient was 1 yr and highest age was 12 years, with the mean age of 7.95 ± 2.8950. 68 (58.1%) patients were male and 49 (41.9%) were female. 48 (41%) patients were Hindu and 69 (59%) were Muslim. 79 (67.5%) patients were from rural background and 38 (32.5%) were from urban area. History of consanguineous marriage among parents was present in 34 (29.1%) patients. Also, family history of seizure disorder was present among 39 (33.3%) patients.

Perinatal factors

Among our study population, 101 (86.3%) were born in hospital and 16 (13.7%) were born at home. 86 (73.5%) patients were delivered normally, 25 (21.4%) were born by caesarean section and 6 (5.1%) patients required assisted delivery. 86 (73.5%) patients cried normally after birth and 31 (26.5%) patients did not cry. History of newborn seizure was present in 21 (17.9%) cases.

Normal developmental milestones were achieved by 84 (71.8%) cases and 33 (28.2%) were abnormal.

Cognitive impairment was present in 54 (46.2%). Total 31 patients had delayed cry at birth. Out of them, 23 patients had cognitive impairment. There is a significant association between delayed cry at birth and cognitive impairment (p value 0.0006).

Clinical factors and seizure semiology

Facial dysmorphism was present in 7 (6%) cases, and neurocutaneous marker was present in 2 (1.7%) cases.

Focal neurodeficit was present in 10 (8.5%) cases and microcephaly in 6 (5.12%) cases.

We observed 53 (45.3%) cases of CPS, 34 (29.1%) cases of CPS with secondary generalization, 28 (23.9%) cases of generalized seizure and 2 (1.7%) cases of simple partial seizure.

Most of the focal seizure cases were extratemporal in origin; 58 cases (49.6%). Only 31 (26.5%) cases were temporal in origin. Aura was absent in majority of patients i.e. 105 (89.7%). Most common aura was auditory and sensory aura, 4 (3.4%) cases each. Clustering of seizure episodes were seen in 12 (10.3%) cases only. Most of the seizures occurred at day time, 73 (62.4%) cases, nocturnal seizures seen in 7 (6%) cases. History of status epilepticus was present in 23 (19.7%) cases.

We applied Cleveland clinic study protocol for seizure semiology classification [11].

Finally, our cohort revealed hypermotor seizures (tonic, clonic, myoclonic, epileptic spasm, atonic, dialeptic, versive and unclassified motor seizures) in 87% cases, hypomotor seizures in 9.4% cases and automotor seizures in 3.4% cases.

Among the hypermotor seizures most common semiology was clonic type, seen in 48 (41%) patients, followed by tonic type, seen in 24 (20.5%) patients. Hypomotor seizure observed in 11 (9.4%) cases. 5 (4.3%) patients had epileptic spasms, 6 (5.1%) patients had atonic seizures, versive seizures were present in 4 (3.4%) patients, unclassified motor seizures in 5 (4.3%) and 7 (6.0%) patients had myoclonic seizures.

We identified 4 cases of west syndrome, 6 cases of SSPE. 1 case of Lennox Gastaut syndrome, Absence epilepsy, myoclonic epilepsy, reflex epilepsy and absence epilepsy and Tuberous sclerosis each.

Semiological seizure type	No of patients
Tonic seizure	24 (20.5%)
Clonic seizure	48 (41.0%)
Tonic clonic seizure	2 (1.7%)
Myoclonic seizure	7 (6.0%)
Atonic seizure	6 (5.1%)
Dialeptic seizure	1 (0.9%)
Versive seizure	4 (3.4%)
Epileptic spasm	5 (4.3%)
Hypomotor seizure	11 (9.4%)
Automotor seizure	4 (3.4%)
Unclassified motor seizure	5 (4.3%)

Table 1: *Semiological seizure type.*

Neuroimaging and EEG

In our study, the etiological diagnosis was made based on MRI brain. The imaging findings were divided into 1) Normal 2) Perinatal encephaloclastic (PEC) conditions, which include hypoxic ischemic encephalopathy (HIE) changes, neonatal hypoglycemic injuries (NHBI), periventricular leucomalacia (PVL), and focal cortical infarcts (FI) 3) Other etiologies like mesial temporal sclerosis, tuberous sclerosis, focal cortical dysplasia, heterotopia etc.

Total 53 (45.3%) patients had normal MRI brain (non lesional) and the imaging was abnormal in 64 patients. 52 (44.4%) of this patients had perinatal hypoxic hypoglycemic injuries to the brain (Gliosis), mesial temporal sclerosis were found in 4 (3.4%) patients, heterotopias were noted in 2 (1.7%), focal cortical dysplasia in 1 (0.9%), Corpus callosal lipoma in 1 (0.9%) patient, cortical tuber in 1 (0.9%) patient, leukodystrophy in 2 (1.7%) patients, Fahr's disease in 1 (0.9%) patient.

Posterior head (occipital, parieto-occipital, parieto-occipital with perirolandic) region were predominantly affected in hypoxic hypoglycaemic injuries of brain.

16 (13.7%) cases had focal interictal epileptiform discharges, 14 (12%) patients had multifocal discharges, periodic complex noted in 6 (5.1%) cases and generalized complex in 6 (5.1%) cases. 75 (64.1%) patients had normal EEG.

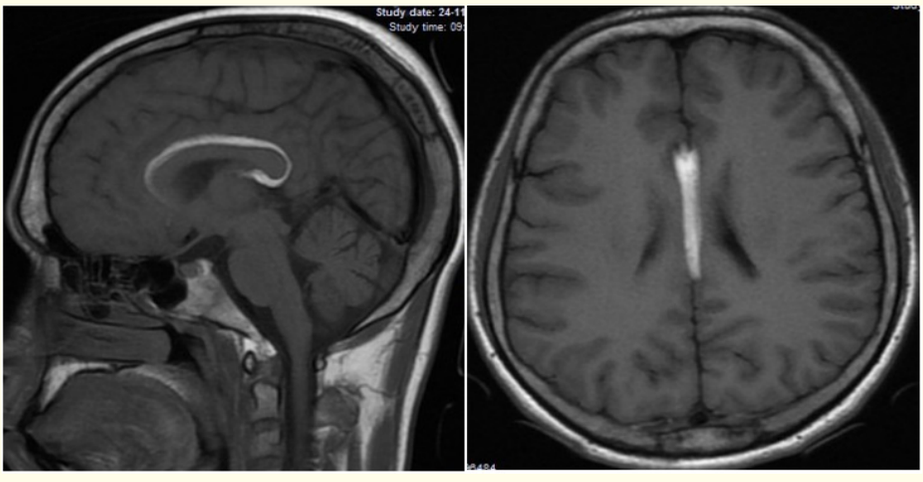

Figure 1: *MRI Brain T1 sagittal and axial sections shows corpus callosal lipoma.*

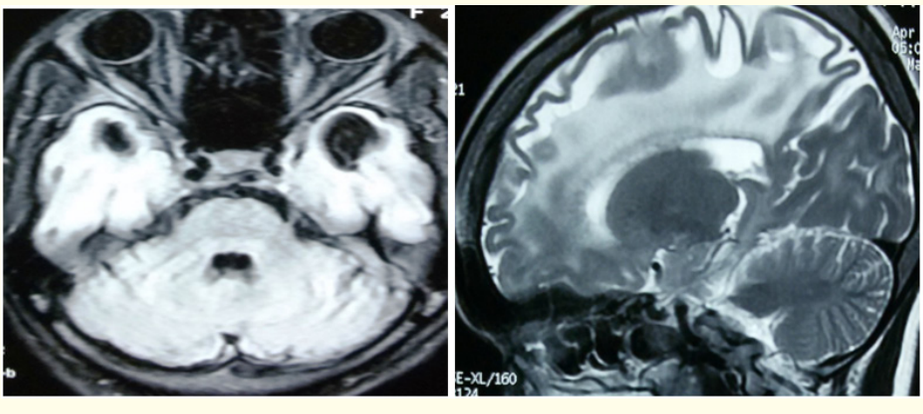

Figure 2: *MRI Brain T2 FLAIR and T2 saaggital sections showing cysts in bilateral temporal and frontal region with white matter changes.*

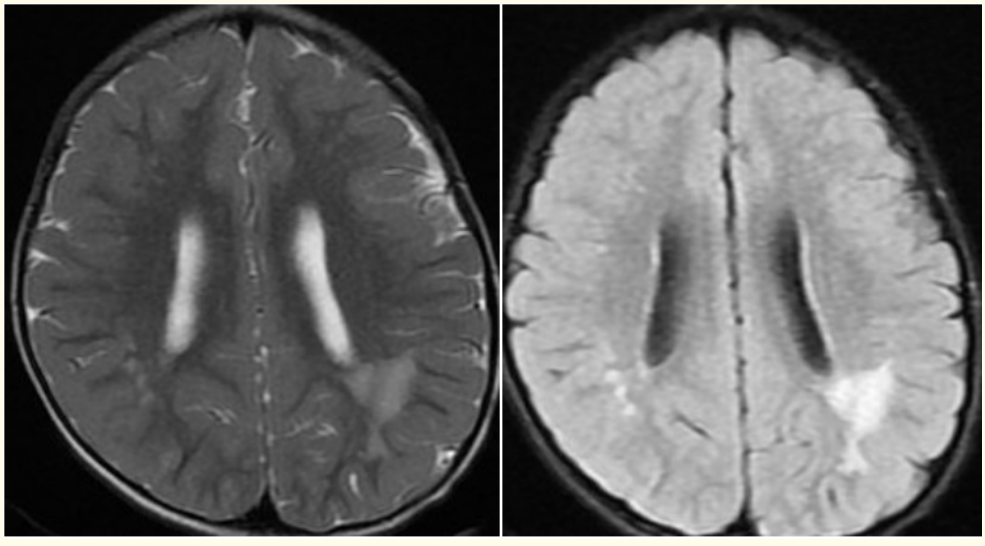

Figure 3: *MRI Brain T2 and FLAIR showing periventricular leukomalacia.*

Relationship between perinatal factors and other determinants

In our study, total 31 patients had delayed cry at birth. Out of them 19 patients had gliosis in MRI. There is a significant association between delayed cry at birth and brain injury (p value- 0.035).

52 patients in our study had evidence of perinatal insult. 40 of these patients were born out of vaginal delivery and 12 patients were delivered by LSCS. The association between mode of delivery and perinatal injuries were not statistically significant (P value 0.82).

The patients with cognitive impairment had perinatal injuries more commonly than patients with normal development (p value- 0.000).

38 out of 58 patients with complex partial seizure of extra temporal origin had imaging evidence of perinatal injuries but only 9 out of 31 patients with complex partial seizure of temporal origin had perinatal injuries. This association is statistically significant (P value- 0.0016).

Details of anti-epileptic drug therapy

Among our study population, 60 (51.3%) patients were on monotherapy and 57 (48.7%) patients were on polytherapy.

In polytherapy group, 41 (35%) cases were on 2 drugs, 11 (9.4%) cases were on 3 drugs, 4 (3.4%) cases on 4 drugs and 1 (0.9%) patient was on 5 drugs. Sodium valproate was used in 69 (59%) cases, carbamazepine was used in 54 (46.2%) cases, phenytoin was used in 15 (12.8%) cases. Phenobarbitone was used in 32 (27.4%) cases, clonazepam and clobazam used in 6 (5.1%) cases each. Levetiracetam was used in 6 (5.1%) cases, diazepam was used in 4 (3.4%) cases.

34 out of 57 patients on polytherapy had imaging evidence of perinatal injuries, whereas 18 out of 60 patients on monotherapy had perinatal injuries. This association is statistically significant (P value- 0.0015).

After treatment, 12 (10.3%) patients became seizure free. Weekly seizure frequency reduced from 18 cases to 3 cases, occasional seizure frequency reduced from 43 cases to 10 cases and half yearly seizure frequency reduced from 8cases to 2 cases.

Treatment gap

We observed treatment gap in 54 (46.2%) cases. Social stigma in 8 patients, lack of parental education in 16 patients, alternative medicines use in 12 patients and cost of the medicines in 18 patients are observed as treatment gap in our study population.

Causes of treatment gap	No of patients
Cost	18 (15.4%)
Lack of parental education	16 (13.7%)
Alternative medicines	12 (10.3%)
Social stigma	8 (6.8%)

Table 2: *Causes of treatment gap.*

Discussion

Demographic profile

In our study, male: female ratio was 1.39:1 and this is similar to a study done by V Udani., *et al.* (M: F-1.8:1). Epilepsy is slightly more common in males than in females but the difference is not statistically significant [12]. Sex of the patient probably did not affect the seizure prognosis.

There were 21 (17.9%) patients with seizure onset in the newborn period. This is in concordance with other studies showing the incidence of epilepsy is high in the infantile population [12,13].

Consanguinity was found in 29.1% of our study population. A study from Kerala has noted 13.5% of consanguinity in children with epilepsy. Frequency of consanguinity in India varies from 15.9% to 32.9% [6].

Family history of seizure was present in 33.3% of our patients. Other studies had documented much lower rates: 24.1%, 13.7%, and 22.2% respectively [13-15]. However, its association with development of epilepsy was significant in other studies by Monetti VC., *et al.* and in a study from Kerala [16,17].

Perinatal factors

In our study, the institutional delivery was 86.3% and home delivery was 13.7%. Out of them, 73.5% of deliveries were normal vaginal delivery and 21.4% deliveries were LSCS delivery. WHO recommended maximum rate of LSCS was 15%. But, 36.2% of LSCS delivery were documented in a study from Italy [18,19]. The association between mode of delivery (LSCS or vaginal) and perinatal injuries were not statistically significant (P value-0.82) in our study.

There was no statistically significant association between place of delivery and perinatal insult (P value-0.42). Even though we expect more significant difference in perinatal insult between home delivery and institutional delivery it was not noted in our study. The reason for this could be due to the fact the level of perinatal care is more important determinant factor than the mode and place of delivery.

A study done by Sarad Kumar Singh., *et al.* concluded that even though hospital delivery has increased significantly in India, the expected decline in perinatal mortality rate (PNMR) was not present [20].

There was a significant association between delayed cry at birth and perinatal injuries in imaging (P value-0.035). Javad Akhondian., *et al.* observed that newborn seizure was 17.6% in children with intractable epilepsy similar to our observation [14]. Francesco Pisani., *et al.* found that moderate HIE with or without newborn seizure was not significantly related to post neonatal epilepsy but severe HIE has [21]. Most of the studies from developed nations did not find any causal relationship between maternal or early neonatal factors and risk for

development of epilepsy [16,22,23]. However, most of the studies from developing countries found these factors to be still relevant [5,6]. This may be due to the reason the etiology of early onset epilepsy is largely different in developed versus developing countries.

Clinical factors

The patients with developmental delay had more perinatal injuries than patients with normal development, which is statistically significant (P value-0.01). The patients with cognitive impairment had more perinatal injuries than patients with normal development (P value-0.000). The presence of developmental delay and cognitive impairment were well documented in literatures which are in concordance with our study [5,15]. More than 75% of children with epilepsy had developmental delay on routine screening by a research group. Age of onset of seizures, frequency and duration of epilepsy are the determinants of cognitive impairment in epilepsy. Focal neurological deficit, microcephaly were also observed in other studies [5]. Children with neonatal hypoglycaemic brain injuries (NHBI) tend to have more number of microcephaly, mental retardation and epilepsy and lower rate of spasticity and dystonia [5]. A similar trend was noted in our study.

Epilepsy

The Cleveland clinic study noted 79% of motor seizures, 20% of hypomotor seizures and 1% of automotor seizure [26]. Mild variation in semiological classification in our study may be due to the reason that we classified the seizures purely on the basis of carefully elicited clinical history rather than ictal Video EEG. Tuqba Hirfanoqlu., *et al.* has done a study of seizure semiological classification based on history from patients and based on video EEG. He compared the consistency of history based classification with video EEG classification. He concluded that the semiological seizure classification based on history can reliably be used in day to day outpatient visits [27].

89 (76.1%) of our cases were having focal epilepsies, 28 (23.9%) cases had generalized epilepsy. In the focal epilepsy group, Complex partial seizure of extra temporal was more commonly observed (49.6%) than temporal origin (26.5%). Dura-Travel T., *et al.* have documented 52.9% focal epilepsy, 43.6% generalized epilepsy and 3.5% had epilepsy with an undermined localization in his study [28].

The higher incidence of generalized epilepsy in the later study could be due to the fact that the age of onset of epilepsy included in the study was up to 15 years.

Most of the perinatal insults were found at the occipital and parieto- occipital regions. This may be the reason for predominance of CPS ET in our study.

Imaging and etiology

Parieto-occipital and occipital region were the common sites of perinatal injuries. Some authors documented parieto-occipital and occipital region were commonly involved in NHBI (neonatal hypoglycemic injuries). In our study, gliosis was found in 52 (44.4%) patients. Whereas only 12 (9.5%) patients had other etiology. This observation is in concordance with other studies [5]. Studies from developed countries found that cortical dysplasia, agyria-pachygyria and tuberous sclerosis are the main etiology for remote symptomatic epilepsy occurring in infancy and early childhood in their population [29].

In this study 54.7% of patients were having symptomatic epilepsies and 45.3% of patients having non lesional epilepsies. This observation is much different from V Udani., *et al.* study in which 83 out of 100 cases were diagnosed to have symptomatic epilepsies and 17 cases were non lesional [5]. Probably, higher tesla MRI may give more information about these non lesional epilepsies in future.

In countries like India, perinatal factors still play a major role in the causation of infantile and early childhood onset remote symptomatic epilepsy. As per the WHO/ILAE estimation, almost 10% of incidental epilepsy can potentially be prevented. Birth asphyxia and neonatal hypoglycemia often coexist and causes severe brain damage [5]. Hence, increasing the institutional deliveries and improving the quality of care during high risk period (pre and perinatal) will go a long way in reducing the perinatal hypoxic- hypoglycemic brain injuries in babies, which will have direct effect in reducing early onset remote symptomatic epilepsy in our part of the country.

A study by Chaurasia., *et al.* showed normal EEG in 60.5% cases among their study population, which is similar to our study [30,31].

Antiepileptic treatment (AED)

Sodium valproate was the most commonly used (59%) in our study, followed by carbamazepine (46.2%) and phenobarbitone (27.4%). 49.60% of our patients receiving polytherapy.

In Glasgow's study 47% new onset epilepsy patients went into freedom with institution of first drug, 13% with second drug and only 4% with third drug [32].

A study from Singapore showed usage of monotherapy in 62.7% and polytherapy in 37.3% cases [33].

Treatment gap

We indentified 54 (46.2%) cases of treatment gap in our study. 15.4% were due to high cost of AED, 13.7% were due to lack of parental education, 10.3% due to alternative medicines usage and 6.8% were due to social stigma.

Mbuba C., *et al.* [34] showed an overall estimate of the treatment gap of 56% and it varies from 22% in urban setting to 90% in villages in Indian context [35]. The reasons for this were cost of treatment 62% (11 - 90%), non-availability of AED 53% (18 - 44%), belief in traditional medicines 44% (6-82%), superstitions and cultural beliefs 40% (7 - 65%) [34].

Summary and Conclusion

Our study empathetically establishes the contribution perinatal hypoxic ischemic injuries as an important cause of the early childhood onset epilepsies. Mode of delivery and Institutional delivery did not have the expected impact in reducing perinatal hypoxic-hypoglycemic brain injuries and it emphasises the need to improve quality perinatal care among institutional deliveries in our country. Delayed cry at birth is a significant independent risk factors for perinatal hypoxic brain injuries and late seizure generation. Focal epilepsy, particularly focal epilepsy of extra temporal origin is the commonest epilepsy type observed. In addition to perinatal brain injuries (44.4%) and other symptomatic epilepsies (10.3%), 45.3% of patients had non lesional epilepsies. Nearly 50% of these epileptic patients require polytherapy for seizure control.

Treatment gap in epilepsy includes cost of therapy, lack of parental education, use of alternative of medicines and social stigma.

Bibliography

1. Simon D Shorvon., *et a*l. "Epilepsy and Related Disorders". Neurology A Queen Square Textbook 2nd: 221-235.
2. Sanjeev V Thomas and Aparna Nair. "Confronting the stigma of epilepsy". *Annals of Indian Academy of Neurology* 14.3 (2011): 158-163.
3. Strzelczyk A., *et al.* "Cost of epilepsy: a systemic review". *Pharmacoeconomics*. 26.6 (2008): 463-476.
4. Mark H Libenson., et al. "Epidemiology of epilepsy, Seizure classification, epilepsy syndromes". Rudolph's Pediatrics 2nd: 2198-2199.
5. V Udani., *et al*. "Neonatal Hypoglycemic Brain Injury-A Common Cause of Infantile-onset Remote Symptomatic Epilepsy." *Indian Paediatrics* 46.2 (2009): 127-132.
6. Thomas Varghese Attumalil., *et al.* "Risk factors of childhood epilepsy in Kerala". *Annals of Indian Academy of Neurology* 14.4 (2011): 283-286.
7. Jagarlapudi Murthy., *et al*. "Determinants of the epilepsy treatment gap in resource limited setting : a study in a rural community in south India". *Neurology* 86.16 (2015).

8. Robert S.Fisher., *et al.* "Epileptic seizures and Epilepsy Definitions proposed by the International League Against Epilepsy (ILAE) and International Bureau for Epilepsy (IBE)". *Epilepsia* 46.4 (2005): 470-472.

9. Bassel W abou-Khalil et al. "Epilepsies, Bradley's Neurology in Clinical Practice 6th edition". Chapter 67:1583.

10. Mohamad A Mikati. "Seizures in Childhood, Nelson Textbook of Pediatrics 19th edition" (2013-2019).

11. H Luders., et al. "Semiological seizure classification". *Epilepsia* 39.9 (1998): 1006-1013.

12. Lars forsgren and Dale Hesdorffer. "Epidemiology and prognosis of epilepsy". The treatment of epilepsy 3rd edition: 21-31.

13. Teodoro Dura-Trave., *et al.* "Incidence of Epilepsies and Epileptic Syndromes Among Children in Navarre, Spain: 2002 Through 2005". *Journal of Child Neurology* 23.8 (2008): 878-882.

14. Javad Akhondian., *et al*. "Predictive factors of pediatric intractable seizures". *Archives of Iranian Medicine* 9.3 (2006): 236-239.

15. Christine M. Freitag., *et al*. "Incidence of epilepsies and Epileptic Syndromes in Children and adolescents: A Population Based Prospective Study in Germany". *Epilepsia* 42.8 (2001): 979-985.

16. Monetti VC., *et al.* "Risk factors for idiopathic generalized seizures: a population based case control study in Coparo, Italy". *Epilepsia* 36.3 (1995): 224-229.

17. Casetta M., *et al.* "Risk factors for cryptogenic and idiopathic partial epilepsy a community based cse control study in Copparo Italy". *Neuro epidemiology* 21.5 (2002): 251-254.

18. Mastaki J Kambale. "Social predictors of caesarian section births in Italy". *African Health Sciences* 11.4 (2011): 560-565.

19. M PAI P Sundram., *et al.* "A high rate of Caesarian section in an affluent section of Chennai: Is it cause for concern?" *Medical Journal of India* 12.4 (1999): 156-157.

20. Sharad Kumar Sngh., *et al.* "Impact of National Health Mission on Perinatal Mortality in rural India". *Indian Pediatrics* 49.2 (2012): 136-139.

21. Francesco Pisani., *et al.* "Development of epilepsy in newborn with moderate hypoxic-ischemic encephalopathy and neonatal seizures". *Brain and Development* 31.1 (2009): 64-68.

22. Tsuboi T Okada S. "Exogenous causes of seizures in children: a population study". *Acta Neurologica Scandinavica* 71.2 (1985): 107-113.

23. Rantakallio P Von Wendt L. "A prospective comparative study of the etiology of cerebral palsy and epilepsy in a one year birth cohort from Northern Finland". *Acta Neurologica Scandinavica* 75.4 (1986): 586-592.

24. Kurtz Z., *et al.* "Epilepsy in young people: 23 year follow up of the British national child development study". *BMJ* 316.7128 (1998): 339-342.

25. Joy D. Desai. "Epilepsy and cognition". *Journal of Pediatric Neurosciences* 3 (2008): 17-29.

26. H M Hamer., *et al*. "Symptomatology of Epileptic Seizures in the First Three Years of Life". *Epilepsia* 40.7 (1999): 837-844.

27. Tuqba Hirfanoqlu M.D. *et al.* "Semiological seizure classification: Before and after Video EEG monitoring of seizures". *Pediatric Neurology* 36.4 (2007): 231-235.

28. Dura-Travel T., *et al.* "A descriptive study of childhood epilepsy". *Revista de Neurología* 44.12 (2007): 720-724.

29. S.V.Thomas., *et al.* "Economical Burden of Epilepsy in India". *Epilepsia* 42.8 (2001) 1052-1062.

30. King MA., *et al*. "Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients". *Lancet* 352.9133 (1998): 1007-1011.

31. R Chaurasia., et al. "Imaging in pediatric epilepsy: spectrum of abnormalities detected on MRI". *Journal of Evolution of Medical and Dental Sciences* 2.19 (2013): 3377-3387.

32. Kwan P and Brodie MJ. "Effectiveness of First Antiepileptic Drug". *Epilepsia* 42.10 (2001): 1255-1260.

33. Shih-Hui., et al. "Pattern of anti-epileptic drug usage in a tertiary referral hospital in Singapore". *Neurological Journal of South East Asia* 2 (1997):77-85.

34. Mbuba CK., *et al*. "The epilepsy treatment gap in developing countries: a systematic review of the magnitude, causes, and intervention strategies". *Epilepsia* 49.9 (2008): 1491-1503.

35. Meyer AC., *et al.* "Global disparities in the epilepsy treatment gap: A systemic review". *Bulletin of the World Health Organization* 88.4 (2010): 260-266.

Volume 11 Issue 6 June 2019