Original Research Article

Investigation of the Clinical presentation and etiological factors of neonatal seizures: A cross-sectional study

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Abstract

Introduction: The occurrence of neonatal seizures per se has been positively correlated with structural brain damage and its consequent sequels at later stages in life. This study was conducted to determine the incidence, etiology, clinical type, and outcome of seizures in newborns hospitalized in neonatal intensive care.**Materials and Methods:** Age on admission for neonates who presented with seizures or later on developed seizures in the hospital varied between 0 days to 25 days with a mean value of 3.1+0.6 days. Among the neonates convulsing in the hospital 58.3% (n=70) comprised of males and 41.6% (n=50) comprised of females. 78.3% (n=94) belonged to rural areas, while as around 16% (n=21.6) were hailing from urban localities. **Results:** Estimation of sample size: Sample size was calculated on the basis of prevalence of neonatal seizures in hospitalized children reported from previous studies of around 4%.The total sample size calculated was around 65, however we decided to take at least 120 patients. Seizure type was diagnosed by clinical observations made by the authors and the resident doctors. The etiology was based on laboratory findings, and /or imaging studies of the brain (ultrasonography, CT scan).**Conclusion:** Biochemical abnormalities were commonly associated with other etiologies like asphyxia, intracranial hemorrhage and meningitis; hence these should be actively sought for and treated for optimal seizure control.

Keywords: Neonatal, seizures, Clinical factor, etiologies.

Introduction

Neonatal seizures are a common neurological problem in neonates with a frequency of 1.5-14/1000 neonates[1]. The occurrence of neonatal seizures per se has been positively correlated with structural brain damage and its consequent sequels at later stages in life. Historically seizures were divided in following clinical categories viz. focal clonic, multifocal clonic, tonic, myoclonic, & subtle seizures[2].Diverse medical conditions in the newborn can be associated with neonatal seizures. Hypoxia-ischemia is nonetheless traditionally considered the most common cause of neonatal seizures[2,3].Seizures during the neonatal period are a considerable problem, not only because they are symptoms of neurologic or metabolic disorder, but also because there is a strong association between them and permanent handicaps in the survivors. The neonatal brain is susceptible to permanent damage as a consequence of the seizures (Wasterlain CG., 1979).Seizures are more usual among neonates than in other age groups, and they influence about 1% of all neonates, with greater frequency in untimely or low birth weight newborns compared to term babies. In the neonatal extensive care gadgets, the prevalence is going as excessive as 10-25% out of which approximately 15% will die and 35-40% could have principal neurological squeal[4].Other causes include intracranial hemorrhage, intracranial infections, metabolic disorders, CNS malformations, birth trauma, drug withdrawal, and less frequent metabolic disorder such as inborn error of metabolism[5]. Seizures are one of the immediate neonatal emergencies, where diagnostic and therapeutic plans are necessary because delay in therapy often results in poor neurological outcome[6].Central nervous system infections during intrapartum or postnatal period can be associated with seizures[9].Biochemical disturbances occur frequently in neonatal seizures either as an underlying cause or as an associated abnormality[7,8].Metabolic disturbances could be more commonly transient and rapidly correctable or less commonly inherited as persistent causes. Infants of diabetic mothers, small for gestational age infants, infants with birth asphyxia are at more risk of hypoglycemia. Late onset hypocalcaemia due to use of high phosphate infant formula has been cited as common cause of seizures[9,10]. However commonly hypocalcaemia occurs in infants with trauma, hemolytic disease, asphyxia and IDM and usually coexists with hypoglycemia and hypomagnesemia[11] and presents at 2-3 days of life. Hypomagnesaemia with serum <1.5 mg/dl can occasionally manifest with tetany and seizures at 2-4 weeks of age and has secondary hypocalcaemia associated. Hypophosphatemia may be caused by ingestion of milk formulas containing high amounts of phosphorous, excessive parenteral administration of phosphorus, impaired renal function, and hypoparathyroidism [12].Hyponatremia as a result of fluid overload renal compromise and SIADH (syndrome of inappropriate ADH secretion) can be a frequent complication of birth asphyxia and could complicate the management of seizures in this condition[13]. Seizures represent the mind's final common response to insult. The preliminary damage may be quick; however, membrane harm release excitotoxic substances such as glutamate, which cause similarly epileptic interest. Magnetic resonance imaging of the brain has shown markedly decreased myelination in youngsters who had suffered from neonatal convulsions[14]. This study was conducted to

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determine the incidence, etiology, clinical type, and outcome of seizures in newborns hospitalized in neonatal intensive care.

Methods

This study was conducted in Department of Pediatrics, IGIMS Patna, India. Estimation of sample size: Sample size was calculated on the basis of prevalence of neonatal seizures in hospitalized children reported from previous studies of around 4%.The total sample size calculated was around 65, however we decided to take at least 120 patients. After taking an informed written consent from the attendants of babies who were admitted in our neonatology section, a total of 120 consecutive neonates within the age group of 0-28 days presenting with seizures from September 2018 to December 2020 were enrolled in the study. The study was approved by the ethics committee of the institution.

Seizure type was diagnosed by clinical observations made by the authors and the resident doctors. The etiology was based on laboratory findings, and /or imaging studies of the brain (ultrasonography, CT scan). The criteria for diagnosing various biochemical disorders were as follows: hypocalcaemia (Ca++<7.0 mg/dl), hypomagnesaemia (Mg++<1.5 mg/dl hypernatremia (Na+<135 mEq/L). Hypoglycemia was diagnosed if blood glucose levels were less than 45 mg/dl in term infants, and less than 40 mg/dl in preterm infants. CSF examination was considered abnormal when there were elevated CSF leukocytes, low CSF sugar, elevated CSF protein and/or positive culture[4,5]. Other non- seizures movements were differentiated from seizures and excluded; exclusion criteria included those with jitteriness or sleep-related muscular activities.In addition complete blood counts, band cell count, absolute neutrophil count, micro-ESR, blood culture, USG cranium, MRI/CT, and CSF analysis were done as per the requirement in individual cases

Statistical analysis

Data was described as mean ± SE and %age. Software used for data analysis was SPSS 16.0 (statistical package for social sciences) and MS Excel**.**

Results

A total of 2570 neonates were admitted during the study period (from the start of study till enrolment of last patient). A total of 120 consecutive babies developed seizures in the study period hence accumulative frequency of around 4.6% was recorded in neonatal seizures in our set up.

A total of 2570 neonates were admitted during the study period. Out of them 1460 were referred to us from peripheral institutions (outborn), while around 1110 neonates were born in our institution (inborn). Seizure frequency of around 3.4% was recorded in inborn neonates, while it was around 5.6% in outborn group.

Table 1: Seizure incidence

Neonates	Total	Seizure	Percentage
Inborn	1110 (43.1%)	38	3.4
Outborn	1460 (56.8%)	82	5.6
Total	2570 (100%)	120	4.6

Age on admission for neonates who presented with seizures or later on developed seizures in the hospital varied between 0 days to 25 days with a mean value of 3.1+0.6 days. Among the neonates convulsing in the hospital 58.3% (n=70) comprised of males and 41.6% (n=50) comprised of females. 78.3% (n=94) belonged to rural areas, while as around 16% (n=21.6) were hailing from urban localities.

Table 2: Socio-demographic characteristics of the neonates with seizures

Socio-demography		n	%
Age on Admission (day)	mean ± SE	3.1 ± 0.6 (0, 27)	
Gender	Male	70	58.3
	Female	50	41.6
Residence	Rural	94	78.3
	Urban	26	21.6

The first day on which the seizures presented had a significant correlation with etiology, on an average presented on 4.3+0.5 days and varied from as early as 1 day to as late as 25 days. Majority of HIE patients presented with neonatal seizures in the first 72 hrs. Intracranial hemorrhage in preterm neonates had a slightly delayed age of presentation usually at or greater than first 72 hrs. Primary metabolic seizures except for late hypocalcaemia had presentation in the first half of first week. Late hypocalcaemia presented around the end of first week.

Table 3: Presenting characteristics of the neonates with neonatal seizures

Characteristic		n	%
Apgar Score at 5min	< 7	54	45.0
	7 to 10	66	55.0
Gestational Age (NBS)	Preterm	45	37.5
	Term	75	62.5
Weight	Appropriate for Gestation Age	75	62.5
	Large for Gestation Age	13	10.8
	Small for Gestation Age	32	26.6
Age of Onset of seizure (day)	mean ± SE	4.3 ± 0.5 (1, 25)	
Head Circumference (cm)	mean ± SE	34.4 ± 0.3(30, 37)	
Length (cm)	mean ± SE	48.1 ± 0.6(42, 53)	

The overall etiological profile comprised of hypoxic ischemic encephalopathy, intracranial haemorrhage, meningitis, metabolic disorders and sepsis in that order. Seizure type and their relative occurrence in different etiologies recorded by clinical observation have been depicted in table 6 and in figure respectively. Tonic seizures and focal clonic seizures each comprised 54.2% (n=9) and 47.3% (n=8) among intracranial haemorrhage.

Table 4: Etiology of the neonatal seizures

Etiology	n	%
Hypoxic Ischemic Encephalopathy	48	40
Intra Cranial Haemorrhage	17	14.1
Meningitis	18	15
Undiagnosed	7	5.8
Primary Metabolic	20	16.6
Septicemia	10	8.3

Focal clonic seizures were commonest seizure type in neonates with meningitis 41% (n=8). 20 neonates (33%) had primary metabolic seizures and 39 (70.2%) neonates had metabolic abnormalities superimposed or coincident on a primary illness like hypoxic ischemic encephalopathy, ICH, meningitis, sepsis etc.

Table 5: Seizure characteristics

Seizure Type	N	%
Focal Clonic	35	29.1
Multi Focal Clonic	22	18.3
Subtle	33	27.5
Tonic	30	25

Discussion

Biochemicals disturbances occur frequently in neonatal seizures either as an underlying cause or as associated abnormalities and are often underdiagnosed, hence the need for this study to determine etiology and biochemical abnormalities in neonatal seizures which would help in early recognition and treatment and hence better prognosis in neonatal seizures. The incidence data which is described around ~4% is the minimum since not all neonates would have attended the hospital. Being a tertiary care and referral hospital in Kashmir it is likely that many neonates managed at primary health centers may never have reached our hospital and we surely are missing them in our hospital attendance. Also the study group included the babies with seizures who were admitted not only in neonatal intensive care unit (NICU) but also in level 2 care nursery. Our center has no facility for continuous EEG monitoring, and we are limited to assessing babies with seizures on clinical grounds alone. Hospital staff and doctors have differing abilities to recognize suspicious behaviours; this variability will lead to over diagnosis or underdiagnosed in the absence of confirmatory continuos videographic EEG. However our incidence rate is similar to 3% shown in studies by Ment et al.[15] and 4.1% by Asindi et al.[16]

The most common metabolic disturbances were hypoglycemia and hypocalcemia, which is consistent with the observations of Fiaz et al.[17] The mortality rate observed in our study was 14.7%, which was higher than that (9%) reported in the study by Ronen et al,[18] but similar to the finding reported by moayedi et al. (13.6%)[19]. This increased mortality may be due to the severity of the etiological factors in newborns with neonatal seizures. HIE and infections are the most common leading causes of mortality in our study and therefore, prevention of asphyxia and treatment of maternal infections can reduce this rate. The most common risk factor of hearing loss were hyperbilirubinemia, asphyxia,birth weight less than 1500 gr, Septicemia, convulsion, and meningitis[20]. The main limitation of this study was unavailability to obtain EEG/aEEG for all neonates with seizure at the time of our study, because EEG plays a crucial role in the evaluation of neonatal seizures.

As posited, efficacy of anticonvulsant therapy is an important issue in occurrence of adverse neurologic outcome and multiple treatments have been suggested[21,22], but the results on the most appropriate drug regimen seem to be controversial [23,24].In the present study, the most commonly used drugs were phenobarbital and phenytoin, which resulted in 36% neurodevelopmental delay, while a higher rate of adverse neurologic outcome are reported by other studies[18,25,26]. Notably, 13 cases in the present study received no treatment by the neurologist's advice and stayed without seizure and without neurodevelopmental delay during follow-up.

Strengths and Limitations: The current study could investigate a combination of clinical, Para clinical and demographic details of neonatal seizure and the adverse neurologic outcome in neonates referred to a central pediatric hospital. Yet, the present study had some limitations, as well. One of the limitations of the current study was the high rate of neonates being discharged by parents, and unwillingness to undergo further examination that resulted in lack of identification of the cause of seizure in several cases, which might have affected the results regarding the etiology of neonatal seizure. In addition, the retrospective nature of the study, beside the fact that data was collected from one center limited the generalizability of data.

Conclusion

Hypoxic ischemic encephalopathy was the commonest etiology of neonatal seizures and in them most of the seizures had an onset in the first 72 hours. Overall focal clonic and subtle seizures were the commonest seizure types encountered. Hypocalcaemia was the commonest biochemical abnormality in primary metabolic seizures. Biochemical abnormalities were commonly associated with other etiologies like asphyxia, intracranial hemorrhage and meningitis; hence these should be actively sought for and treated for optimal seizure control.

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