Original Research Article

Clinico-etiological profile of seizures in term and near-term neonates: tertiary care hospital based observational study

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Received: 10 October 2017

Accepted: 13 October 2017

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ABSTRACT

Background: Neonatal period is very important for development of immature brain and it is also most vulnerable period for development of seizures. Seizures have varied etiology as well as presentation during neonatal period. Considering this we planned this study with objective of finding incidence, etiology, type and time of onset of seizures and their correlation along with short term outcome.

Methods: It is a prospective observational study done in level 2 NICU set up of Government Medical College from November 2008 to September 2009. Total 115 term and near term neonates (≥ 35 weeks of gestation) presenting in NICU with seizures were enrolled in study. All relevant details were recorded on performa and investigations were sent. Data was described as mean $\pm$ SD and %. SPSS 13 software was used as data analysis.

Results: Incidence of seizures came out to be 6.1% of total NICU admission, which was more in male appropriate for gestational age (AGA) babies and those who were born vaginally, extramural and to primiparous mother. Birth asphyxia was most common etiology of seizures and majority presented within 24 hours of birth and meningitis was most important cause of seizure after 7 days of life. Subtle seizures were most common clinical type of seizure in the present study. Risk factor for poor neurological outcome came out to be Hypoxic Ischemic Encephalopathy (HIE).

Conclusions: Hypoxic ischemic encephalopathy was most important etiology of neonatal seizures and most important risk factor for poor neurological outcome and subtle seizures being most common clinical type of seizure.

Keywords: Asphyxia, Etiology, Neonatal seizures

INTRODUCTION

Seizures occur more frequently in neonatal period as compared to any other period of life.¹ During neonatal period seizures are distinct and most important clinical presentation of neurological involvement.¹ Frequency of neonatal seizures varies from 1.5-14/1000 neonates or 1-2% of admission to NICU.² Seizure in neonates is usually presentation of underlying clinical disorder or rarely it can also be due to primary epileptic disorder.³ Most common etiology of neonatal seizures is considered to be hypoxic ischemic encephalopathy followed by

intracranial hemorrhage, neonatal meningitis, various metabolic disorders, cerebral infarction and neonatal epileptic syndromes.⁴⁻⁸ Natural history of seizure is unknown, but observation suggests that seizures may be most severe in first week of life and subsequently abates regardless of intervention. Onset of seizures has also been correlated with etiology of seizures in various studies. Clinical presentation of seizures is also varied and is divided historically into focal clonic, multifocal clonic, tonic, subtle and myoclonic. The effect of neonatal seizure on brain development is difficult to differentiate from those of the brain lesion causing them. However

recent data from animal studies suggest that seizures themselves are deleterious to the development of immature brain.^{9,10} Changes in neuromotor function observed during the first 3 months of life are closely related to the maturation of central nervous system and the presence and absence of brain damage. Hence it is important to detect abnormalities in neurodevelopment as early as possible so that early intervention can be done to achieve better outcome.¹¹

Due to high prevalence of neonatal seizures and mortality and morbidity related to them this study was planned to determine - common etiology of neonatal seizures, most common clinical presentation of seizures and to correlate neurological outcome at 3 months of age with etiology and severity of seizures.

METHODS

This prospective observational study was conducted at level 2 neonatal intensive care unit (NICU) of Department of Pediatrics LLRM Medical College Meerut from November 2008 to September 2009 after taking ethical clearance from ethical committee of college. Sample size was calculated as per the prevalence of neonatal seizures reported in previous studies that is around 4%. Sample size calculated was around 65 but we decided to include all neonates presenting with seizures during that duration that was 115.

Study population included all term and near-term neonates $\geq$ 35 weeks of gestation admitted in NICU with clinically apparent seizures.

Clinical criteria for diagnosis of seizures were

- Unifocal, multifocal or generalized clonic movements
- Tonic posturing
- Spontaneous paroxysmal, repetitive motor or autonomic phenomenon like lip smacking, chewing, paddling, cyclic movements or respiratory irregularities classified as subtle seizures.

All resident doctors posted in NICU were trained for 4 days with the help of video demonstration and lectures regarding classification and diagnosis of seizures clinically by a neonatologist in our department. Neonates with uncertain clinical manifestations or those who had first seizures after 28 days of life were excluded from the study.

After obtaining written and informed consent from attendants of patient all neonates fulfilling inclusion criteria were enrolled in the study. Detailed maternal history including maternal medical history, antenatal history - illness during pregnancy, drug intake, radiation exposure, leaking or bleeding per vagina, evidence of fetal distress and natal history - APGAR score, type of delivery, duration of labor, requirement of resuscitation

were recorded on a pre-structured performa along with base line characteristics of convulsing neonate (age, sex, gestational age, weight, length and head circumference). Details of seizure episode including age of onset, time taken to control, type of seizure and etiology of seizure when confirmed after history examination and investigations were also recorded on performa. Seizure episodes were managed as per the NICU protocol. After ensuring airway patency and circulation samples for blood glucose, serum calcium, sodium and potassium levels were sent before instituting specific anticonvulsants. Magnesium and phosphorus could not be done due to unavailability of these investigations at our institute. Biochemical abnormalities were diagnosed as per following criteria¹²

- Hypoglycemia: Blood sugar <40 mg/dl
- Hypocalcemia: Total serum calcium <7 mg/dl or ionized serum calcium <4 mg/dl
- Hyponatremia: Serum sodium >150 meq/dl
- Hyponatremia: Serum sodium <130 meq/dl
- Hyperkalemia: Serum potassium >5.5 meq/dl
- Hypokalemia: Serum potassium <3.5 meq/dl.

Other investigations as per requirement of the suspected diagnosis of neonate were done including septic screen, blood cultures, CSF analysis, and USG cranium, MRI or CT scan.

Neonates who were discharged successfully from NICU were called for neurological assessment at 3 months of age other than their regular follow up. Outcome was assessed by achievement of milestones appropriate for that age (social smile, mother recognition), tone assessment by Amiel Tison method (adductor angle, popliteal angle, dorsiflexion angle and scarf sign). Head circumference, feeding, weight gain, activity of child, neonatal reflexes and persistence of seizures were also assessed. Neurodevelopmental outcome was considered abnormal if milestones were not achieved or if tone of baby was not falling in range of Amiel Tison score. Data was observed as mean, median and percentages and SPSS 13 software was used for data analysis.

RESULTS

During study period from the time of start of study till enrollment of last patient 1864 patients were admitted in our NICU. Out of them 115 patients developed seizures either during course of hospital stay or at the time of admission hence cumulative frequency of seizures in the present study came out to be 6.1% of total NICU admissions.

Base line characteristics of neonates enrolled in study is as described in Table 1. Out of 115 cases incidence of seizures was more in male babies as compared to females, neonates who were AGA, born to primiparous mother, delivered vaginally and extramural also had significant high seizure incidence.

Table 1: Base line characteristic variables of participants.

Parameters	Observations	P value
Gestational age* (weeks)	38.6 (1.45)	
Length* (cm)	48.4 (0.3)	
Head circumference* (cm)	32.9 (0.1)	
Weight (Kg)		
AGA	81	<0.05
SGA	34	
Gender		
Male	79 (68.69)	< 0.05
Female	36 (31.3)	
Parity		
Primiparous	74 (64.34)	<0.05
Multiparous	41 (35.65)	
Mode of delivery		
Vaginal	84(73.04)	<0.05
LSCS	31 (26.95)	
Place of delivery		
IM Hospital	34 (29.56)	<0.05
EM Hospital	65 (56.52)	
EM Home	16 (13.91)	

Value indicates mean (SD)* or number (%); AGA: Appropriate for gestational age; SGA: Small for gestational age; IM: Intramural; EM: Extramural

Etiological profile of seizures in the present study includes hypoxic ischemic encephalopathy (HIE), meningitis, intracranial hemorrhage (ICH), hypoglycemia, hypocalcaemia, kernicterus and undiagnosed in order as in Table 2. Subtle seizure was most common clinical type of seizure observed during our study (46.08%) followed by generalized tonic (39.13%), focal clonic (0.09%), multifocal clonic (0.03%) and focal clonic (0.01%). On correlating etiology with type of seizures, HIE and ICH presented predominantly with subtle and generalized tonic seizures, meningitis resulted in subtle, generalized tonic and focal clonic type of seizure while kernicterus caused generalized tonic and focal clonic type of seizures (Table 2).

Seizures were observed to occur in first 24 hours in maximum cases of HIE, majority of cases of meningitis presented with onset after 7 days, in kernicterus it was between 3-7 days (Table 2). Out of 115 babies enrolled in study 29 expired during NICU stay, 13 were lost to follow up 73 babies were followed up at 3 months of age. Normal neurological outcome was 75% in cases with meningitis, 80% in HIE 2 and only 11% in HIE 3. On bivariate analysis risk factor for poor outcome was HIE 3 with odds ratio 72 and 95% confidence interval (5.7-908.9).

Table 2: Clinico-etiological profile of seizures.

Etiology	n (%)	Day of onset of seizures (%)				Type of seizures (%)				
		0-1	1-2	3-7	>7	Subtle	Gen tonic	Focal clonic	Multifocal clonic	Focal tonic
HIE	85 (73.91)	78	4	18	0	47	41	7	4	1
Meningitis	14 (12.1)	22	0	11	67	33	50	11	6	0
Intracranial Haemorrhage	6 (0.052)	0	60	40	0	50	50	0	0	0
Hypoglycaemia	4 (0.034)	50	0	50	0	100	0	0	0	0
Hypocalcaemia	2 (0.017)	50	0	0	50	50	0	50	0	0
Undiagnosed	2 (0.017)	50	50	0	0	0	50	50	0	0
Kernicterus	2 (0.017)	0	0	100	0	0	50	50	0	0

DISCUSSION

In the present study of clinic-etiological profile of neonatal seizures in term and near-term neonates we found incidence of neonatal seizure in our NICU set up to be 6.1% of NICU admission which is comparable with studies of Mentet al and Asindi et al who reported incidence of 3% and 4.1% respectively.^{13,14} Singh M reported incidence of neonatal seizures of 0.5% to 0.8%.¹⁵ Reported incidence by Lanska et al is 2.84 per 1000 live birth. Erikson et al and Seay and Bray reported 20% incidence of seizure activity in neonates admitted to NICU.^{16,17} Our reported incidence could also have been

higher if we would have included preterms in the present study as reported incidence in preterms is higher as compared to terms.¹⁸ Our study center had no facility for confirmatory continuous video graphic EEG monitoring hence diagnosis of seizures was made on the basis of clinical findings hence differing abilities of doctors to recognize seizures can be one of the cause for over and under diagnosis of seizures.

In the present study we found overall male sex preponderance in neonates who developed seizures which is similar to other studies like Cockburn et al, Fredrichsen, McIntyre et al and Bagla et al.¹⁹⁻²² Reason for this sex preponderance is not explainable but may be

attributed to some extent to male sex preponderance in our society as male babies are more cared for and immediate medical attention is given to them.

Majority of babies in the present study were appropriate for gestational age, this can be explained as birth asphyxia being major cause of seizures in our study is more common in newborns with good weight and also those with good weight have more chances of survival before reaching hospital. Vaginal and extramural delivery and babies born to primiparous mother all are risk factors themselves for developing birth asphyxia hence presented more with seizures. Birth asphyxia was most important cause of seizures in our study, although we did not have elaborate investigation panel to diagnose specific inborn error of metabolism though they are assumed to be rare. Sood A et al and Kumar A et al reported birth asphyxia as etiology of seizures in 45.71% and 48.2% cases respectively which is less than as reported in the present study might be because as we included only term newborns and being a tertiary care referral center, we received maximum extramural babies including home delivery too which is a predisposing factor to develop asphyxia.^{23,24}

Subtle seizures are most common pattern of seizure in this study as also reported by other authors.^{22,24,25} Meningitis and kernicterus presented with generalized tonic seizures in our study which is not documented in other studies. However, Kumar et al found multifocal clonic seizures as most common pattern which is rare in our study and found only in birth asphyxia and meningitis.¹² In present study seizure onset within 48 hours is mainly due to birth asphyxia followed by intracranial hemorrhage and those who presented after 7 days is due to meningitis being a part of late onset sepsis followed by late onset hypocalcemia. High incidence of seizures in first week of life as compared to later weeks is similar to findings of Eriksson et al and Bagla et al and can be explained by birth asphyxia being most important cause of seizures.^{16,22}

In the present study approximately 25% babies expired during NICU stay. Over one third of these babies were delivered at home and no resuscitation facilities were accessible to them at birth. High mortality rates were most likely due to receiving babies in NICU in critical stage of illness and seeking late care in level 2 NICU with no ventilation facilities available. Although in previous studies also high mortality rates have been reported by authors in patients in HIE 3.²⁶ Outcome at 3 months in our study is also comparable to other studies. As reported by Robertson and Finer neurological outcome was 100% normal in mild HIE, 71% normal in moderate HIE, while none were normal in severe HIE.²⁷ According to previous studies, in meningitis by both group B *streptococcus* and gram-negative bacilli, 50% survivors had no sequelae, 40% had mild to moderate sequelae while only 10% had severe sequelae.²⁸⁻³⁰

Present study was a prospective observational study with complete records of patients and following NICU protocols for seizure managements, still lack of continuous EEG monitoring, not a multicentric study and lack of advanced metabolic tests to confirm diagnosis of undiagnosed seizures are limitation of the present study. Hence there is a need of future studies to be done taking care of all limitations of the present study.

CONCLUSION

Present study reports incidence of seizures to be 6.1% of NICU admission with over all preponderance of seizures in male sex, extramural and vaginal deliveries. Birth asphyxia, early onset seizures and subtle seizures being more common. HIE 3 came out to be only risk factor for short term abnormal neurological outcome on bivariate analysis.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Verma G, Shamsi S, Pathak U. Clinico-etiological profile of seizures in term and near-term neonates: tertiary care hospital based observational study. *Int J Contemp Pediatr* 2017;4:xxx-xx.