

Clinical Profile and Etiology of Neonatal Seizures in a Tertiary Care Hospital in North India

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ABSTRACT

Introduction: Seizures are more common in the neonatal period than in any other stage and affects approximately 1% of all neonates. Amongst neurological disorders, seizures are the most common in neonates. The study was conducted to determine the etiology and clinical profile of neonatal seizures.

Material and methods: A hospital based prospective observational study was undertaken in the Post graduate Department of Pediatrics, G.B. Pant Hospital, which is a referral hospital of Government Medical College, Srinagar for children. A total of 104 neonates presenting with seizures or who developed seizures in our hospital from 01 April 2015 to 31 March 2016 were enrolled in the study.

Results: HIE was the commonest etiology of neonatal seizures (61.5%) followed by Meningitis (12.5%), Intracranial hemorrhage (7.7%) and Primary metabolic disturbances (10.5%). ICH was more common in preterm babies than in term babies. Majority of patients presented with seizures in the first 72 hours of life. In HIE most of the patients presented within first 24 hours of life. In Meningitis seizures were common after 72 hours of life.

Conclusion: In most of the cases, the causes of neonatal seizures were present. Birth asphyxia was the main etiology identified. However, the burden of neonatal seizures due to asphyxia is much more in our valley than has been observed by other studies in other parts of the world especially in western countries.

Keywords: Neonatal Seizures, Etiology, Clinical Profile

INTRODUCTION

Seizures are more common in the neonatal period than in any other stage and affects approximately 1% of all neonates.¹ Amongst neurological disorders, seizures are the most common in the neonates.²

A seizure is defined clinically as a paroxysmal alteration in neurologic function, i.e. motor, behavior and/or autonomic function. The fundamental mechanisms of neonatal seizures are generally unknown, disturbance in energy production can result in a failure of Na⁺/ K⁺ pump. In addition to these cellular factors, differential development of neural systems may enhance the excitatory state of the immature brain and predispose to seizures. Other suggested mechanisms of injury include effects of nitric oxide synthase inhibition on cerebral circulation, which then contributes to ischemic injury.³

The International League Against Epilepsy classification adopted by WHO, still considers neonatal seizures within an unclassified category.⁴ Historically seizures were divided

in following clinical categories viz focal clonic, multifocal clonic, tonic, myoclonic, and subtle seizures.⁵

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.^{6,5} Cerebral infarction and stroke are the second most common cause of neonatal seizures occurring in otherwise well term infants, without previous risk factors.⁷ Hypoglycemia is a well-known cause of neonatal seizures. Infants with sepsis and meningitis frequently have hypoglycemia which can be attributed to inadequate intake, increased metabolic rate and impaired ability to metabolize glucose.⁸

Hypocalcemia is total serum Ca levels <7mg/dl although the exact level at which seizure occurs is debatable. Late onset hypocalcemia due to use of high phosphate infant formula has been cited as common cause of seizures.^{9,10} However commonly hypocalcemia occurs in infants with trauma, hemolytic disease, asphyxia and IDM and usually coexist with hypoglycemia and hypomagnesemia and presents at 2-3 days of life. Hypomagnesemia with serum <1.5mg/dl can occasionally manifest with tetany and seizures at 2-4 weeks of age and has secondary hypocalcemia associated. Mg depletion is known to predispose to decreased PTH secretion. Hyperphosphatemia may be caused by ingestion of milk formulas containing high amounts of phosphorous, excessive parenteral administration of phosphorus, impaired renal function, and hypoparathyroidism.

Hyponatremia as a result of fluid overload, renal compromise and SIADH (syndrome of inappropriate ADH secretion) can be a frequent complication of birth asphyxia.

Outcome is predicted by the underlying aetiology.¹¹ Patients

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with hypoxic ischemic encephalopathy (HIE), intraventricular hemorrhage and structural brain malformation have the worst prognosis.^{11,12} while those with transient metabolic abnormalities and benign idiopathic or familial etiologies have the best prognosis.¹³

Current research aimed to study the etiology of neonatal seizures and to study the clinical profile of neonatal seizures.

MATERIAL AND METHODS

A hospital based prospective observational study was undertaken in the Post graduate Department of Pediatrics, G.B. Pant Hospital, which is a referral hospital of Government Medical College, Srinagar for children.

A total of 104 neonates presenting with seizures or who developed seizures in hospital from 01 April 2015 to 31 March 2016 were enrolled in the study.

All neonates (age 0 – 28 days) who presented to the hospital with history of seizures or who develop seizures during the course of hospital stay were taken into study.

Detailed antenatal history examination and clinical details of each seizure episode reported by the mother and subsequently observed by the resident doctors on duty were recorded. Blood sugar was done and venous blood was collected as soon as possible and blood glucose, total serum calcium levels, Na⁺, K⁺, Mg and Phosphorus levels were done immediately after baby had seizures and before instituting any treatment. In addition complete blood counts, blood culture, USG cranium, MRI/CT, CSF analysis, serum lactate and ammonia, TMS, urinary GCMS and TORCH antibody titres were done as per the requirement in individual cases.

STATISTICAL ANALYSIS

Data was entered in a Microsoft excel spreadsheet. Continuous variables were summarized as mean and standard deviation. Categorical variables were summarized as percentage.

RESULTS

A total number of 5128 neonates, 4890 term and 238 Preterm, were admitted in the newborn care unit of the P.G. Department of pediatrics, G.B. Pant hospital, during the study period which extended from 1st April 2015 to 31st March 2016. Out of these, 104 neonates were diagnosed as having neonatal seizures. A hospital based seizure prevalence of 2.03% was thus observed. However in Preterm babies this prevalence was much higher at 11.76% (table-1).

Residence

Among these 84 patients (81%) were from rural areas and 20 patients (19%) were from urban areas.

Sex distribution

Males comprised 58 patients and females comprised 46 patients **Gestational age**

Out of 104 neonates admitted with seizures, 76 (73.1%) were term and 28 (26.9%) were preterm.

Maternal characteristics (table-2)

Maternal age

Extremes of maternal age viz. ≤ 18 years or ≥ 40 years

comprised 7%, while 93% comprised in the age group of 19-39 years.

Parity

53% (n=55) neonates were born to nulliparous women, while parous women comprised 47% (n=49).

Mode of delivery

39.4% (n=41) of cases were born by caesarean section while 60.4% (n=41) were born by vaginal delivery.

Age of onset of seizures (table-3)

Majority of neonatal seizures occurred within the first few days of life, with first 03 days accounting for 76% of neonatal seizures.

In HIE seizures occurred in the first few days of life with majority occurring in the first 24 hours of life. In our study 61% of seizures due to HIE occurred within first 24 hours of life and 92% of seizures occurred within 48 hours of birth.

In meningitis seizures were more common after first 3 days of life. 92% of seizures occurred after 3rd day of life, among these 30% cases presented after 1st week of life.

		n	%
Gender	Male	58	55.8
	Female	46	44.2
Gestational age	Very preterm	1	1
	Moderate preterm	7	6.7
	Late preterm	20	19.2
	Term	76	73.1
	Post term	0	0
Birth weight	Normal	67	64.5
	Low birth weight	37	35.5

Table-1: Presenting characteristics of the casesj

Characteristic		N	%
Maternal Age	≤ 18	1	1
	19 to 29	53	51
	30 to 39	44	42.3
	≥ 40	6	5.8
Maternal Parity	Nulliparous	49	47.1
	Parous	55	52.9
Delivery Type	Caesarean Section	41	39.4
	Routine Vaginal	63	60.6
Labour Record Foetal Distress		24	23.1

Table-2: Maternal Characteristics of the Neonates

Etiology	n	Percent
HIE	64	61.5
ICH	8	7.7
Meningitis	13	12.5
TORCH infections	1	1.0
Hypocalcemia	6	5.8
Hypoglycemia	4	3.8
Hypomagnesemia	1	1.0
IEM	1	1.0
Epilepsy syndromes	1	1.0
Unknown	5	4.8

Table-3: Etiology of neonatal seizures

Gestation		HIE	ICH	Meningitis	Hypocalcemia	Hypoglycemia
Term	n	53	3	9	3	2
	% of total cases	70	4	12	4	3
Preterm	n	11	5	4	3	2
	% of total cases	39	17.8	14	11	7

Table-4: Distribution of various etiologies among Term and Preterm neonates

Metabolic abnormality	Term	Preterm
Hypocalcemia	3	3
Hypoglycemia	2	2
Hypomagnesemia	0	1

Table-5: Distribution of primary metabolic seizures among Term and Preterm neonates

		Patients showing Metabolic Abnormality	Hypocalcemia	Hypoglycemia	Hypomagnesemia	Hyponatremia	Hypertremia	Hypokalemia	Hyperkalemia
Primary Metabolic Seizures	N	11	6	4	1	0	0	0	0
Non-Metabolic Seizures	N	46	22	14	2	3	1	3	1
Total	N	57	28	18	3	3	1	3	1

Table-6: Overall Biochemical Profile in Patients with Neonatal Seizures

Hypocalcemic seizures had a dual distribution regarding the age of onset. In preterm neonates Hypocalcemic seizures were more common in the first 72 hours of life. In neonates who had hypocalcemia, likely due to high phosphate formula feeds, seizures occurred after first week of life (table-4,5).

Type of seizures

Subtle seizures were the most common type of neonatal seizures present in 37% cases (n=39) followed by focal clonic 25% (n=26), multifocal clonic 15% (n=16), focal tonic 10% (n=10), myoclonic 10% (n=10).

The most common seizure type in HIE were subtle seizures which were present in 33% neonates followed by focal clonic in 25% and multifocal clonic seizures in 22% of cases. Generalized tonic seizures were the most common type of seizures in ICH occurring in 37% cases

In meningitis the most common type of seizures were subtle seizures involving 46% of cases

Subtle seizures were also the most common type in hypocalcemia occurring in 83% cases and focal clonic seizures occurring in the rest 17% neonates.

Hypoxic Ischemic Encephalopathy was the most common cause of neonatal seizures comprising 61.5% (n=64) of cases. Out of 64 cases, 53 neonates (83%) were term and 10 (17%) were preterm.

The second most common cause was CNS infections with meningitis comprising 12.5% (n=13) and 1% due to TORCH infections (01 case which was due to toxoplasmosis).

Intracranial hemorrhages (ICH) on the whole comprised 7.7% (n=8) of cases, but in Preterm population it was responsible for about 18% of seizures.

Metabolic causes were responsible for 10.5% (n=11) of neonatal seizures. Hypocalcemia was the most common metabolic abnormality responsible for 5.8% (n=6) of neonatal seizures followed by hypoglycemia 3.8% (n=4). Seizures due to metabolic disturbances were more common in preterm babies than in term babies. There were 05 cases of neonatal seizures which were undiagnosed comprising 4.8% of total cases (table-6).

DISCUSSION

The present study was conducted in the Post-graduate Department of Pediatrics, G.B. Pant hospital, an associated hospital of Government Medical College Srinagar, a tertiary care hospital receiving patients from entire Kashmir valley and some adjoining parts of Jammu and Ladakh regions.

It was a hospital based observational study conducted over a period of 01 year from 1st April 2015 to 31st March 2016. A total of 104 neonates were enrolled in our study.

We noted a hospital based prevalence rate of 2.03% which is comparable to 3% shown in studies by Ment et al²⁴ and 4.1% by Asindi et al.²⁵ who used continuous EEG monitoring, reported seizures in as many as 25% of neonatal admissions. The difference between these studies and our study is because our centre has no facility for continuous EEG monitoring, and we are limited to assessing babies with seizures on clinical grounds alone.

In preterm babies we noted a hospital based prevalence of 11.7% as compared to overall prevalence of 2.03%.

We found neonatal seizures slightly more common in males with a male to female ratio of 1.26:1. The studies of neonatal seizures by Tekgul H. et al¹⁶ showed male to female ratio of

1.15:1.0 and 1.7:1 respectively which is similar to our study. Another study conducted by Sabzehei MK et al¹⁷ in the same hospital found it to be more common in males.

In our study subtle seizures constituted 37% of cases where as focal clonic seizures were present in 25% of neonates, multifocal clonic in 15% and tonic seizures in 13% of neonates. Rose et al¹⁸ found that 40.6% had subtle seizures and 8.9% had tonic seizures and 35.5% had clonic seizures. In our study 76% cases presented with seizures within the first 72 hours of life. Rose et al¹⁸ also found early onset seizures in 50.33% babies whereas Coen RW et al¹⁹ found that 81% of babies had early onset seizures.

Frequency of HIE as a cause of neonatal seizures was 61.5% in our study. Nawab T et al²⁰ also reported Birth asphyxia in 60% cases which is similar to our study. The high frequency of Birth asphyxia as a cause of neonatal seizures in our set up is because obstetric and newborn care facilities are inadequate in many of the peripheral health facilities in our valley. Also, facilities for transferring such babies are unsatisfactory. These shortcomings may predispose more to birth asphyxia and its sequelae and may predispose the babies to infection and other metabolic complications like hypoglycemia.

In our study Meningitis as a cause for neonatal seizures accounts for around 12.5% cases. A study conducted by Legido A et al²¹ reported that out of 40 babies 17.2% had some kind of infection leading to fits. Our results are comparable to these studies.

Intracranial hemorrhage was there in 7.7% cases in our study. Bushra A et al²² reported that ICH was there in around 9.5% of cases, quite comparable to our study. Incidence of ICH was much higher in preterm than term neonates.

Primary metabolic seizures were seen in about 10.5% cases in our study. Hypocalcemia constituted 54.5% of metabolic causes followed by hypoglycemia which represented around 36% of metabolic seizures. Calciolari²³ reported 8 cases of neonatal seizures with primary metabolic abnormality, among them 4 (50%) were due to hypocalcemia, 3 (38%) due to hypoglycemia and 1 (12.5%) due to hyponatremia. The results of our study are comparable to these studies.

There were 05 (4.8%) undiagnosed cases in our study. Although CT head was done in all these cases but no CNS malformation was detected on CT scans. As our hospital doesn't have an MRI facility so it couldn't be done during the hospital stay of these cases.

The main limitation of this study was unavailability to obtain EEG/aEEG in neonates suspected to have seizures, as our hospital doesn't have such a facility. Because of it we might have missed a number of cases who had non- epileptic seizures.

CONCLUSION

Majority of patients presented with seizures in the first 72 hours of life. In HIE most of the patients presented within first 24 hours of life. In Meningitis seizures were common after 72 hours of life. Subtle seizures were the commonest seizure type observed, followed by focal clonic seizures.

Generalized tonic seizures were the most common type of seizures in ICH. Around 55% neonates had a biochemical abnormality either alone or in association with other etiologies. Secondary metabolic abnormalities were most common in HIE. Hypocalcemia was the commonest biochemical abnormality in primary metabolic seizures. Hypoglycemia was the next most common abnormality

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