



Original Research Article

Neonatal Seizure – Etiological & Clinical differentiation

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ABSTRACT

A seizure in the neonatal period is an emergency that reflects potentially significant insults to the immature brain. Seizure represents the most distinctive signal of neurological disease in the newborn period and they are most frequent of the major manifestation of neonatal neurological disorder.

It is critical to recognise neonatal seizures, determine their etiology and to treat them promptly.

The neonatal period is one of high seizure hazard for a number of reasons. The last trimester and early neonatal period are characterized by rapid brain growth and development; both structure and function undergo substantial changes in relatively short time. This process has specific metabolic demand, substrate requirements and the need to proceed under relatively ideal conditions. Unfortunately the neonatal period is also characterised by a wide range of factors that can negatively impact this process; there are many diverse pathological process and disorders that may occur frequently and that may cause brain dysfunction. In addition the relative excitability of the immature brain compared with that of older children or adults make the neonate more prone to seizure. As regards the aetiological factors in neonatal seizures they are many; some of them require multiple sophisticated investigations, while others can be diagnosed clinically with a few simple investigation. Thus in present perspective, neonatal seizure deserves intensive investigation and comprehensive research.

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1. Aims and Objectives

To find out different clinical patterns of neonatal seizure and their etiology and contributing factors in relationship with birth weight and gestational age.

2. Materials and Methods

The current study was carried out on all neonate, who got admitted with seizure or developed seizure subsequently during hospitalisation in nursery ward, M.K.C.G. Medical college hospital, Berhampur, Odisha during period April 2018 to April 2020. All the mothers of the neonate with seizure were interviewed about antenatal check up and any disease during pregnancy were taken, detail description on present delivery were also inquired. Special emphasis on neonates regarding time of first cry and feeding pattern and

exact time of onset seizure following birth, its pattern and presence of any other abnormal behaviour as noticed by mother. All babies were weighed unclothed. Gestational age was determined by maternal history of L.M.P. by Naegill's method. Modified dubowitch method was used when exact history was not available. A detail physical examination was carried out on all the neonates, 48 hrs after the last seizure, in naked state, under day light. Special vigilance was exercised on detection of pallor, jaundice, oedema, physical malformation, cutaneous rash, nevi or vascular malformation, cataract and organomegaly. It was followed by neurological examination of the neonate when awake but not crying. It consists of examination of skull and spine with head circumference, cranial nerve, muscle tone and superficial, deep and primitive reflexes to find out presence of any neurological deficit. Observed seizure pattern as noticed prior to intervention was recorded and classified as subtle, tonic, focal, clonic and myoclonic varieties with

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subtle variety sub divided into bicycling, eye deviation, buccolingual was followed.

Venous blood sample for hematological and biochemical examination was collected in sterilised vials as soon as possible after the hospitalisation and prior to therapy. The hematological investigation include WBC count including band cells: mature neutrophil ratio, total leucocyte count, peripheral smear examination for any dysmorphic polymorphs, micro ESR & C-reactive protein estimation. The serum level of calcium, magnesium, sodium, phosphorous & blood glucose estimated by precipitation method, atomic absorption spectrometry, flame photometry and glucose oxidase method respectively. Blood sample was collected in glucose broth and after incubation for 24hr samples were subcultured on blood agar and Mac-Conkey agar. Buffy coat smear examination, by gram staining of buffy layer of the blood obtained after centrifugation and separation of plasma was employed for rapid identification of microorganism.

Neonates born before 37 weeks were termed as preterm while those after 37 weeks as term babies. But babies of 42 weeks or more gestational age were nomenclatured as post term. Newborn weighing between 10th and 90th centile are normal, below 10th centile are small for gestational age and above 90th centile are large for gestational age.

Diagnosis of sepsis was done following Desai 1984 criteria compromised of 3 or more hematological abnormalities like band cell: total neutrophil ratio>0.2, total leucocyte count <5000, positive CRP (5mg/ml), micro ESR >10 mm in 1st hr. meningitis was considered in cases of sepsis on basis of low glucose, raised protein and markedly increased cell count in CSF. The criteria for diagnosis various biochemical abnormalities were as follows: hypocalcemia (<7mg/dl), hypomagnesemia (<1.2mg/dl), hypernatremia (>150mmol/dl), hypoglycaemia was diagnosed if blood glucose were less than 45mg/dl.

3. Results

The following observation made among the 90 newborn babies taken into consideration.

Table 1 reveals that out of 90 cases of neonatal seizure studied, 36 were due to HIE and 7 due to primary ICH. Kernicterus, malformation and HDN each had constituted 3,2 and 1 cases respectively. Out of 15 cases of infective origin, 9 had meningitis and 6 had septicaemia. Hypoglycaemia, hypocalcemia and hyponatremia was seen in 10,11 and 2 cases respectively. Neither isolated hypomagnesemia nor hypernatremia was found to be cause of neonatal seizure in any of the neonates under study. Exact cause of seizure could not be determined in 10 neonates. The ratio of preterm to term was 33:57 indicating that term babies are more prone to seizure. No neonates with seizure was born at or after 42weeks of gestation.

Table 2 suggests that despite 16 primary causes of metabolic abnormalities, secondary biochemical alteration had been associated with different primary causes. Out of 18 (50%) cases of HIE with different secondary biochemical abnormalities, hyponatremia was recorded in 10 cases, while hypocalcemia, hyperphosphatemia and hypomagnesemia and hypoglycaemia was observed in 4,2,1 and 8 cases respectively. Similarly in ICH group 3 babies had hyponatremia and one had hypoglycaemia. Meningitis cases (9) too showed hyponatremia in 4 cases and hypoglycaemia in 1 case. One septicaemia baby had recovered hypoglycaemia.

Table 3 Shows subtle seizure as the most common form of seizure in preterm babies. Multifocal clonic is the commonest variety of seizure in term neonates, it was observed in 20 term neonates. Myoclonus was observed mostly in preterm babies, clonic as well as tonic seizures had almost equally distributed among preterm and term babies.

Table 4 showing multifocal clonic, focal clonic, myoclonic, tonic patterns were observed in 40, 22, 29, 13 and 19 cases respectively. Maximum number of subtle and clonic seizures occurred in HIE group. Meningitis and late onset hypocalcemia presented predominantly as multifocal clonic seizures.

4. Discussion

Hypoxic ischemic encephalopathy was found to be the commonest cause of neonatal seizure in this study, with 36 out of 90 cases of seizure had HIE and thus HIE was responsible for neonatal seizure in 40% of total case. This is similar to the finding of Kumar et al.¹ where 45 of neonatal convulsion were due to HIE. The percentage of cases of neonatal seizure due to HIE was 32% in Kelloway and Mirzrahi series (1995) from Texas children hospital. The higher percentage of HIE in Indian studies may be due to a higher prevalence of risk factors of birth asphyxia in developing countries than in developed countries (Kumar R.A., 1995).

Occurrence of hypoglycaemia, hypocalcemia and hyponatremia were recorded in 10(62%), 11(68%) and 2(12%) instances out of 16 cases with primary metabolic alteration. In this group 7 babies had shown simultaneous occurrence of both hypoglycaemia and hypocalcemia. This is similar to observation of Kumar et al.¹ where hyponatremia occurred in 10% cases while hypoglycaemia and hypocalcemia both occurred in 55% of his cases.

In the neonatal seizure group of infection origin 9 cases(60%) were due to meningitis while rest 6 cases(40%) were caused by septicaemia.

No cases of seizure showing hypernatremia nor hypomagnesemia was detected.

Seizure had occurred in 33(36.6%) preterm as against 57(63.3%) term neonates. No baby with seizure had gestational age of 42 weeks or more. This corroborates

Table 1: Distribution of various etiology among preterm and term neonates

Etiology	Pre-term		Term		Total	
	No.	%	No.	%	No.	%
HIE	7	19.40	29	80.50	36	100.00
Primary ICH	6	85.00	1	14.20	7	100.00
Infection						
i)meningitis	3	33.33	6	6.66	9	100.00
ii)septicaemia	4	66.66	2	33.33	6	100.00
Primary metabolic						
i)hypoglycaemia	3	30.00	7	70.00	10	100.00
ii)hypocalcemia	2	18.18	9	81.81	11	100.00
iii)hyponatremia	2	100.00			2	100.00
Kernicterus	2	66.66	1	33.33	3	100.00
Malformation	1	50.00	1	50.00	2	100.00
HDN	0	0.00	1	100.00	1	100.00
Unknown	3	30.00	7	70.00	10	100.00
Total	33	36.66	57	63.33	90	100.00

Table 2: Biochemical abnormalities in neonates with seizure

Etiology	Total no. of cases	Neonates with metabolic disturbances	Hyponatremic	Hypocalcemic	Hyperphosphatemia	Hypomagnesemia	Hypoglycemia
HIE	36	18 (50.0%)	10 (27.7%)	4 (11.1%)	2 (5.5%)	1 (2.7%)	8 (22.2%)
ICH	7	4 (57.1%)	3 (42.8%)	–	–	–	1 (14.2%)
Meningitis	9	5 (55.5%)	4 (44.4%)	–	–	–	1 (11.1%)
Septicemia	6	1 (16.6%)	–	–	–	–	1 (16.6%)
Metabolic	16	16 (100%)	2 (12.5%)	11 (68.8%)	–	–	10 (62.5%)

Table 3: Distribution of different clinical types of neonatal seizures in preterm and term neonates

Clinical type	Preterm (n=33)		Term (n=57)	
	No.	%	No.	%
Subtle	26	78.78	14	24.50
Multifocal clonic	2	6.00	20	35.00
Focal clonic	14	42.42	15	26.30
Myoclonic	11	33.33	3	5.20
Tonic	8	24.24	11	19.20

Table 4: Different clinical patterns associated with different etiologies of neonatal seizure

Etiology	Subtle	Multifocal clonic	Focal clonic	myoclonic	tonic	total
HIE	12 (33.3%)	5 (13.8%)	9 (25.0%)	7 (19.4%)	6 (16.6%)	36 (100%)
ICH	5 (71.0%)	1 (14.2%)	–	2 (28.5%)	4 (57.1%)	7 (100%)
Meningitis	4 (44.4%)	5 (55.5%)	2 (22.2%)	2 (22.2%)	2 (22.2%)	9 (100%)
Septicemia	4 (66.6%)	2 (33.3%)	2 (33.3%)	–	–	6 (100%)
Hypoglycemia	9 (90.0%)	1 (10.0%)	5 (50.0%)	–	3 (30.0%)	10 (100%)
Early	1 (14.2%)	1 (14.2%)	2 (28.5%)	–	3 (42.8%)	7 (100%)
Hypocalcemia						
Late	–	4 (100%)	–	–	–	4 (100%)
Hypocalcemia						
Hyponatremia	1 (50.0%)	–	2 (100%)	–	–	3 (100%)
Kernicterus	2 (66.6%)	1 (33.3%)	1 (33.3%)	–	–	3 (100%)
Malformation	–	–	–	1 (50.0%)	1 (50.0%)	2 (100%)
HDN	–	–	1 (100%)	–	–	1 (100%)
Unknown	2 (20.0%)	2 (20.0%)	5 (50.0%)	1 (10.0%)	–	10 (100%)
Total	40 (44.4%)	22 (24.4%)	29 (32.2%)	13 (14.4%)	19 (21.1%)	90 (100%)

well with Goldberg 1983 study² revealing 34% of neonatal seizure affecting the preterm babies.

Secondary alteration in primary causes of seizure (Table 2) were recorded in 18/36 (50%); 4/7 (57%); 5/9 (56%) and 1/6 (17%) cases of HIE, ICH, meningitis and septicaemia respectively. Hypocalcemia with or without hypomagnesemia and hyperphosphatemia occurred in 4/36 (11%) cases of HIE and was in close correlation with findings from western literature by Erikson, 1979 with 12.5% cases.³ Hypoglycaemia was observed in 8/36 (22%), 1/7 (14%), 1/9 (11%), 1/6 (16.6%) cases of HIE, ICH, meningitis and septicaemia. Hypoglycemia in seizing babies with infective aetiologies were attributed to inadequate intake and increased metabolic rate. Hyponatremia was observed in 10/36 (27%), 3/7 (43%), 4/9 (44%) case of HIE, ICH and meningitis respectively. Similar observation made by Kumar et al. and it was attributed to the syndrome of inappropriate antidiuretic hormone secretion in sick babies.

Table 3 reflected that subtle and myoclonic are more commonly seen among preterm compared to term babies with relative incidence of 26/40 (65%) and 11/14 (80%) respectively. This was in accordance with Scher (1989).⁴ Focal clonic and tonic seizures are seen equally in preterm and term neonates. Multifocal clonic seizures were commonly seen in term neonates.

Table 4 Shows that HIE and meningitis were associated with all form of seizure patterns. In HIE focal clonic and subtle varieties of seizures were commonly observed, they constituted, 9/36 (25%) and 12/36 (33%). Rest constituted as myoclonic 7/36 (19.4%), tonic 6/36 (16.6%) and multifocal clonic 5/36 (14%) cases. In ICH subtle seizure was commonest clinical pattern with incidence of 5/7 (71%) case followed by tonic seizure in 4/7 (57%) cases. Hypocalcemia of early and late onset varieties showed multifocal clonic in 5/11 (45%) and tonic in 3/11 (27%) predominantly. Overall analysis revealed that subtle seizure was the commonest clinical pattern seen in 40/90 (44 cases) and was in close correlation with similar findings by Scher (1989) who found it in 33% of cases.⁴ Multiple type of seizure pattern was commonly seen in many babies.

5. Conclusion

In the present study of 90 neonates with seizure 33 (36.6%) were pre term while rest 57 (63.33%) were term babies. HIE was the commonest cause of seizure present in 36 cases (44%). The frequency of other causes were primary ICH, infection, primary metabolic disturbances and malformations in 8%, 17%, 18%, and 2.2% cases respectively. The exact cause remained undetermined in 11% cases. Relative frequency of hypoglycaemia, hypocalcemia, hyponatremia cases were 62%, 68%, and 12.5% respectively. No seizure of primary hypomagnesemia and hypernatremia origin was found. ICH, hyponatremia, kernicterus cases were seen mostly in preterm with relative

frequency of 86%, 100% and 66% respectively.

Secondary biochemical abnormalities had occurred in 18 (50%), 4 (57%), 5 (55%) and 1 (16%) cases of HIE, ICH, meningitis and septicaemia respectively. The incidence of hypoglycaemia, hypocalcemia and hyponatremia in HIE cases were 8, 4 and 10 respectively.

Most frequent type of seizure observed was subtle variety. Meningitis, HIE cases had shown all patterns of seizure viz. clonic, subtle, myoclonic, tonic and multifocal clonic. Other common pattern being subtle in ICH (71%) and hypoglycaemia (90%). Tonic in early onset hypocalcemia and multifocal clonic in 100% late onset hypocalcemia.

6. Summary

Based on the observation HIE with secondary biochemical abnormalities was the commonest direct cause of neonatal seizures. In addition to bring down the high incidence of primary metabolic abnormalities as another important cause of neonatal seizures, promotion of early and exclusive breast feeding through adoption of baby friendly hospital policy.

Moreover practise of early rooming in will possibly allow early clinical diagnosis of seizures by the mothers themselves.

A detail examination of all neonate is a mandate to look for any cutaneous markers, facial dysmorphism, microcephaly, syndromic manifestation at least once after the baby is stable following delivery.

7. Source of Funding

None.

8. Conflict of Interest

None.

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