

## Study on Profile of Neonatal Seizures with Special Biochemical Profiles Abnormalities in NICU

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### Abstract:

**Background:** Neonatal seizures are clinically significant because very few are idiopathic. Biochemical disturbances occur frequently in neonatal seizures either as an underlying cause or as associated abnormalities. In their presence it is difficult to control seizures and there is a risk of further brain damage.

**Methodology:** The present study included 110 neonates presenting with seizures admitted to NICU at BMIMS, Pawapuri. Study duration of Two years. Detailed antenatal, natal and postnatal history were taken and examination of baby was done and HIE staged according to modified Sarnat's staging. Relevant investigations including biochemical parameters were done and etiology of neonatal seizures and their associated biochemical abnormalities were diagnosed.

**Conclusion:** Biochemical abnormalities are common in neonatal seizures. Isolated biochemical abnormalities without other co morbid states were seen in 13 (11.8%) cases. 33 (30%) cases of neonatal seizures with identifiable etiology had associated biochemical abnormalities.

**Keywords:** Neonatal seizures, Hypoglycemia, Hypocalcaemia; Hypomagnesemia, Hypoxic ischaemic encephalopathy.

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### Introduction

Neonatal seizures represent the most distinctive signal of neurological disease in the newborn period. The convulsive phenomenon are the most frequent of the overt manifestation of neonatal neurological disorders and they are clinically significant because very few are idiopathic. Neonatal seizures differ considerably from seizures observed in older children, principally because the immature brain is less capable of propagating generalized or organized electrical discharges. Since neonatal seizures have an adverse effect on neurodevelopment and can predispose to cognitive and behavioural epileptic complications later in life, prompt diagnostic and therapeutic plans are necessary. It is critical to recognize neonatal seizures to determine their etiology and to treat them for 3 major reasons:

1. First, seizures are usually related to significant illness, sometimes requiring specific therapy.
2. Second, neonatal seizures may interfere with important supportive measures, such as alimentation and assisted respiration for associated disorders.
3. Third, experimental data give reason for

concern that the seizures per se maybe a cause of brain injury

Seizures present with varying manifestations like generalized tonic, multifocal clonic and subtle activity. Therefore, it is important to recognize them and treat it, as delay in recognition and treatment may lead to brain damage. The time of onset of seizure has relationship with the etiology and prognosis. For example, birth asphyxia usually presents in the first three days of life whereas meningitis presents after first week. If the baby convulses within hours of delivery, it signifies poor prognosis and brain damage. The presence of seizure does not constitute a diagnosis but it is a symptom of an underlying central nervous system disorder due to systemic or biochemical disturbances. Biochemical disturbances occur frequently in the neonatal seizures either as an underlying cause or as an associated abnormality. In their presence, it is difficult to control seizure and there is a risk of further brain damage. Among metabolic causes hypoglycaemia, hypocalcaemia, hypomagnesemia, and hyponatremia are commonly seen. Early recognition and treatment of these biochemical disturbances is essential for optimal management and satisfactory long-term outcome.

Taking above points into consideration, the study on clinical profile of neonatal seizures with special reference to biochemical abnormalities has a significant role.

**Objectives**

To assess the biochemical abnormalities in neonatal seizures.

To evaluate the clinical presentation, time of onset and its relation to etiology of neonatal seizures.

**Materials and Methods**

The present study included 110 neonates presenting with seizures admitted to NICU of Bhagwan Mahavir Institute of Medical Science, Pawapuri. Study duration of Two years.

**Inclusion Criteria**

Neonates (first 28 days of life) presenting with at least one of the following clinical type of seizures:

- Generalized tonic seizures.
- Multifocal clonic seizures
- Focal clonic seizures
- Myoclonic seizures

Neonates with seizures who were delivered at our hospital as well as outborn babies were included in the study.

**Exclusion Criteria**

Neonates with isolated subtle phenomenon, apnea or paroxysmal autonomic changes, i.e., only subtle motor movements or apnea without tachycardia were excluded from the study.

Jitteriness in neonates.

Tetanic spasms in neonates.

Detailed antenatal, natal and post-natal history were taken as per the proforma enclosed.

Age & parity of mother were noted. History of whether regular antenatal checkups were done or not was enquired. History of medical illness like diabetes, fever during first trimester or third trimester were asked. History of obstetric complications like PIH, eclampsia, antepartum hemorrhage, oligo or polyhydramnios were taken.

History of PROM, prolonged second stage of labour, Meconium staining of liquor, place of delivery, type of delivery and indication for forceps and caesarean section, were enquired. After delivery whether baby

cried immediately or not, was it meconium stained and any resuscitation done, were enquired. If Apgar score was done, it was noted. The neonate was diagnosed with birth asphyxia if baby did not cry for more than three minutes after birth or documented apgar score was  $\leq 3$  at one minute and  $<7$  at 5 minutes of birth.

**Post-natal History:** History of lethargy, poor feeding, jaundice, excessive cry, fever, vomiting and seizures were taken.

**History of Seizures:** The day of onset of seizures, type of seizures, the duration of seizures, number of seizures and consciousness during and between seizures were taken. The neonatal seizures were classified according to Volpe's classification into multifocal, clonic, focal tonic, tonic and myoclonic.

Hypocalcaemia was defined when total serum calcium  $<7.0$ mg/dL, and Hypercalcemia  $>11$  mg/dl, Hypomagnesemia when serum Mg  $< 1.5$  mg/dL, Hypermagnesemia  $>3$  mg/dL, Hypophosphatemia when serum Phosphorus  $<3.5$ mg/dl and Hyperphosphatemia when serum P  $>8.0$  mg/dl, Hyponatremia when S. Na  $<135$  meq/L and hypernatremia when S. Na  $> 160$  meq/L. Hypokalemia – K  $< 3.5$  meq/l and Hyperkalemia – K  $> 5.5$  meq/l CSF analysis: If septicemia or meningitis was suspected, LP was done and CSF analyzed for color, turbidity, protein, sugar, CRP, total and differential cell count and culture. Other metabolic screening like serum ammonia and serum lactate was done if particular metabolic disease was suspected.

**Statistical Methods:** Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean  $\pm$  SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

**Results**

There were 110 neonates admitted to NICU of Bhagwan Mahavir Institute of Medical Science, Pawapuri. Study duration of Two years. with neonatal seizures.

**Gestational age**

**Table 1: Distribution of Neonatal Seizures according to gestational age**

Gestation of age	No. of cases	%
Term appropriate for gestational age	89	80.9
Term Small for gestational age	11	10.0
Pre term	8	7.3
Post term	2	1.8
Total	110	100.0

In the present study, out of 110 babies 100 were full term, of which 89 (80.9%) were AGA and 11 (10%) SGA. There were 8 (7.9%) preterm and 2 (1.89%) postterm babies.

**Table 2: Sex wise distribution of neonatal seizures**

Gender	No. of cases	%
Male	70	63.6
Female	40	36.4
Total	110	100.0

In our study, 70 (64%) were males and 40(36%) were female babies with male to female ratio of 1.7:1.

**Table 3: Place of delivery of babies with neonatal seizures**

Place of Delivery	No. of cases	%
Home	4	3.6
Hospital	106	96.4
Total	110	100.0

Out of 110 cases, 4 (3.6%) were born at home and 106 (96.4%) were hospital deliveries.

**Table 4: Etiology of seizures**

Etiology	No. of cases (n=110)	%
Birth asphyxia	66	60.0
Septicemia	25	22.7
Metabolic	13	11.8
ICH	2	1.8
Structural	1	0.9
Unknown	3	2.7
Total	110	100

Birth asphyxia is the commonest cause of neonatal seizures in our study. 66 (60%) babies had birth asphyxia, 25 (22.7%) had neonatal meningitis, 13(11.8%) had pure metabolic disorders, 2 (1.8%) babies had intracranial haemorrhage, 1 baby had structural anomaly of partial agenesis of corpus callosum. In rest 3 (2.7%) cases no cause was identified.

Chi squared for onset of seizures on first three days and more than three days with etiology –  $\chi^2 = 72.86$  with p value of  $< 0.001$  (statistically highly significant for onset of seizures on first three days of life with birth asphyxia). The onset of seizures on first day was seen in 59 neonates out of which 54(91.5%) were due to birth asphyxia. On 2nd day 14 babies developed seizures and 10 (71.4%) were due to birth asphyxia, two were due to hypoglycemia alone, 1 was due to hypocalcemia and one was due to congenital anomaly. Late onset seizures ( $>8$  days) out of 16 cases 14(87.4%) were due to neonatal meningitis and is statistically highly significant (p value  $< 0.001$ ) Metabolic abnormalities were seen in 46 cases, of which 33 were non- metabolic seizures and 13 were pure metabolic seizures. The most common biochemical abnormality detected in neonatal seizures in our study was hypoglycemia 19 (41.4%), 9 cases seen only metabolic seizures and 10 with non metabolic. While in metabolic seizures hypoglycemia 9 (69.3%) cases was most common, 13(39.4%) cases of non-metabolic seizures had hyponatremia. There were 13 (11.8%) pure metabolic seizures in our study. In preterm, 2 (22.2%) cases had hypoglycemia. In term AGA one had hypocalcemia, 1 had combined hypocalcaemia and hypomagnesemia, and 3(33.4%) had hypoglycemia. Two term

SGA had hypocalcemia and 4(44.4%) SGA had hypoglycemia. Of the 33 cases of non-metabolic seizures, which showed biochemical abnormality, hyponatraemia was most common abnormality with 13 (39.5%) cases. 10(47.7%) were due to HIE and 3 (30%) cases due to neonatal meningitis. HIE was associated with hypomagnesemia in 2 (9.5%) cases, hypermagnesium in 1 (4.7%) cases and 10 (3.4%) of hyponatremia and 5 (23.9%) cases hypoglycemia. One (50%) case of ICH was associated with hypomagnesemia and 1 (50%) with hypomagnesemia of the 10 cases of neonatal meningitis associated with biochemical abnormalities, 5 (50%) cases were associated with hypoglycemia and 3 (30%) hyponatremia and 1 each of hypocalcemia and hypomagnesemia.

### Discussion

In the present study, 110 neonates with seizures were studied in one and half years period. Both in-born and outborn babies admitted to the NICU with neonatal seizures were included in the study. Neonatal seizures in relation with gestational age, In our study, out of 110 neonates with seizures, 100 (90.9%) were full term neonates, of which 90(81.9%) were appropriate for gestational age and 11(10%) were small for gestational age. Eight (7.3%) were preterm and two babies (1.8%) were post term babies. Majority of neonates with seizures in our study were full term babies and birth asphyxia was the commonest cause of seizures in full term babies and was associated with perinatal complications like MSAF in 23 cases and prolonged 2<sup>nd</sup> stage of labour in 13 cases. Similar observations were seen in a study by Moayed AR et al.

[1] where term AGA babies were 83.6% and preterm were 12.7% and post term 3.6%. Study by Ravneet Sandhu et al. [2] showed AGA babies 81.2% followed by preterm babies 18.8% which is similar to our study. Neonatal seizures have no sex predilection. However, in our study, male to female ratio was 1.75:1, similar with the study of neonatal seizures by Moayedi AR et al. [1] where male to female ratio was 1.3:1. The study of neonatal seizures by Hasan Tekgul et al. [3] showed male to female ratio of 1.15:1.

**Birth weight:** In our study, 72 (65.5%) cases had birth weight >2.5 kg. 23 (20.9%) were between 2 and 2.5 kg and 15 (13.6%) between 1 and 2 kg.

Study by Moayedi AR et al.<sup>1</sup> also showed similar finding of 73.6% >2.5 kg and 22.7% were <2.5 kg. In our study, majority of neonates with seizures were born by normal vaginal delivery 70(63.6%) followed by LSCS 35(31.8%) b and outlet forceps delivery 5 (4.5%). In a study of neonatal seizures by Lakhra Mahaveer et al. [4] 68.7% were born by normal vaginal delivery, 28.1% by LSCS and 3.1% by forceps delivery.

**Day of Onset of Seizures:** In our study, 61(55.5%) neonates out of 110 neonates with seizures had onset within the first day of life. 13 (11.8%) on day 2 and 7 (6.4%) on day 3 of life i.e. 67% within 48 hours and 86.3% within 1 week. Fifteen (13.6%) neonates had late onset seizures that is after 8 days of life to 28 days of life. In a study of neonatal seizures by Ajay Kumar et al. [5] 75% of seizure episodes occurred before 115 hours of age and 57.8% developed seizure within first 48 hours of life. In a study of neonatal seizures by Ronen Gabriel et al. [6] onset of seizures on the first day of life was 36%, 64% had onset of seizures within first 48 hours and 83% within first week of life, which is similar to our study. In the present study, 52 (47.3%) babies had subtle seizures either in the form of oro-buccal movements, eye blinking, cycling movements of limbs or apnoea associated with tachycardia or hypertension. Focal clonic type seen in 21 babies (19.1%), multifocal clonic in 15 cases (13.6%), generalised tonic seizures was observed in 12 (10.9%) cases followed by 10 (9%) babies having mixed type of seizures. In a study of neonatal seizures by Ajay Kumar et al. 46.55% were subtle seizures and 21.55% were generalised tonic seizures. In a study of neonatal seizures by Brunquell Philip J et al. [7] subtle seizures were the commonest occurring in 51% (27 of 53), followed by focal clonic (42%), multifocal clonic (30%) and GTS (23%) which is similar to our study. Lakra Mahaveer et al. [4] also reported that subtle seizures were the commonest. Moayedi AR et al also reported subtle seizures as the commonest seizure. Birth asphyxiated babies developed seizures usually within first 72 hours and more so within first 24 hours and babies with seizures within 24 hours have poor prognosis. Finer MM et

al [8] showed that 48% of infants having seizures within 24 hours were significantly handicapped compared to 24% whose seizures began after 24 hours. Study conducted by Kumar et al. and Arvind Sood et al. [9] showed that biochemical abnormalities were seen in cases of HIE, intracranial bleed and infections which is similar to our study. Kumar et al. [10] showed hyponatremia as most common biochemical abnormality in HIE and hypomagnesemia in 2 cases and hypoglycaemia in 4 cases. But study by Arvind Sood et al. Showed HIE, hypoglycaemia as commonest abnormality followed by hypocalcaemia, hypomagnesemia and hyponatremia. CNS infections in our study were associated with hyponatremia in 3 cases, 5 cases of hypoglycemia and 1 case of hypocalcaemia and 1 case of hypomagnesemia. Kumar et al. also showed similar findings while Arvind et al. showed that intracranial infections were associated with hypocalcaemia and hyponatremia in 2 cases each. Neonates with birth asphyxia may have inappropriate secretion of antidiuretic hormones. We also found hyponatremia in infants with intracranial hemorrhage, meningitis which can be explained again on the basis of inappropriate secretion of antidiuretic hormone seen in these conditions. Hypomagnesemia can be attributed to transient functional hypoparathyroidism while hypermagnesemia was probably due to injection magnesium sulphate given to mother in eclampsia. Hypoglycaemia was seen only in 5 cases of birth asphyxia unlike Ericksson Met al. [11] who showed most cases of HIE are associated with hypoglycaemia. In a study of hypoglycemia by Lilien Lawrence D et al. [12] 41% of hypoglycemic neonates were SGA babies. In a study of hypoglycaemia in neonates by Singhal PK et al. [13] showed, of 2248 babies preterm babies had 3 times increased risk (12.8%) as compared to term babies (3.6%) for hypoglycaemia and that (30.2%) manifest as seizures. In our study, two preterm babies had neonatal seizures and were diagnosed as IVH on ultrasound cranium and CSF study. Preterm neonates are prone for intraventricular hemorrhage because of fragile blood vessels and ineffective supporting structure for periventricular blood vessels.

## Conclusion

Neonatal seizures typically signal underlying significant neurological disease and represent non-specific response of the immature nervous system to varied insults. They are unique and distinctive when compared to seizures in adults because of the immaturity of the nervous system and require separate classification. Isolated metabolic disorders showed 13 cases (11.8%) with biochemical abnormalities with hypoglycemia being the most common followed by hypocalcaemia and 33(30%) cases of neonatal seizures with identifiable etiology had associated biochemical abnormalities with hyponatremia accounting for 13 cases in the group. Recognition of

hypomagnesemia with hypocalcaemia is important because administration of calcium can cause the serum magnesium to drop further and maintain the convulsive state.

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