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**Original Research Article**

# Clinical, etiological, biochemical, microbiological and neurosonogram factors in related with neonatal seizures in Visakhapatnam, India

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## ABSTRACT

**Background:** Neonatal seizure is a common neurological problem in the neonatal period. Detection of seizure, its etiology, and clinical types is important for guiding therapy. A varied number of conditions are capable of causing seizures in the neonatal period. The aim was to study biochemical, microbiological and, nurosonogram factors related with neonatal seizures in Visakhapatanam, India.
**Methods:** The study was carried out in the Department of Paediatrics, Andhra medical college, King George Hospital, Visakhapatnam, Andhra Pradesh. The study was done to assess the biochemical changes, nurosonogram factors and microbilogical organisms implicated in neonatal seizures.
**Results:** The present study is descriptive in nature where clinical spectrum of neonatal seizures in neonates was studied. 1500 neonates were admitted in NICU during the study period, among them 200 (13.3%) developed neonatal seizures. Etiology in majority of the cases of neonatal seizures was hypoxic ischemic encephalopathy (45%) followed in frequency by intracranial haemorrhage (14%), meningitis (12%), hypoglycaemia (11%), hypocalcaemia (4%) and others (14%). The most common organism implicated in neonatal seizures was *Escherichia coli* (36%), followed by *Klebsiella* (30%), *staphylococcus aureus* (19%), *Streptococci agalactiae (*7%) and unknown (8%). Meningitis accounted for 12% of neonatal seizures. Most common biochemical abnormalities noted were hypoglycemia, hypocalcaemia and hyponatremia.
**Conclusions:** Biochemical abnormalities may significantly contribute to seizure activity and possibly correction of these abnormalities may play a significant role in seizure control. A biochemical work up is necessary for all cases of neonatal seizures. Appropriate treatment with antibiotics is essential. Examination of cerebrospinal fluid is essential work up in cases of neonatal seizures. Neurosonogram had good potential in predicting neurological outcome in neonates with perinatal asphyxia. Neurosonogram should be incorporated in the routine evaluation of seizures.

**Keywords:** Biochemical, Microbiological, Neonatal seizures, Neurosonogram

## INTRODUCTION

Seizure is defined as a paroxysmal, time limited change in motor activity and/or behaviour that results from abnormal activity in the brain. Neonatal seizure is a common neurological problem in the neonatal period. Neonatal seizures have always been a topic of interest because of its universal occurrence. A varied number of conditions are capable of causing seizures in the neonatal period the highest incidence of neonatal seizures occurs during first 24 hours of life.[1] Prompt diagnosis, investigations and treatment are vital as delayed recognition of a treatable cause can have a significant impact on child's subsequent neurological outcome.[2] Neonatal seizures often signal an underlying ominous neurological condition, most commonly hypoxic

ischemia. The other common aetiologies of neonatal seizures are intra-ventricular haemorrhage or intra-parenchymal haemorrhage, meningitis, sepsis or metabolic disorders.[3] Seizures cause synaptic reorganisation with aberrant growth (mossy fibres) and may interfere with normal synaptic pruning that takes place during development. If seizures are not controlled, the electrical activity may continue to circulate, a phenomenon called kindling.[4]

The presence of seizure does not constitute a diagnosis but is a symptom of an underlying central nervous system disorder due to systemic or biochemical disturbances or infection.[5]

The objective of this study was to study the etiology of neonatal seizures, to evaluate neonatal seizures with reference to biochemical changes. Microbiological investigation to find the most common organisms implicated in neonatal seizures. And study the factors associated with normal and abnormal developmental outcome with reference to etiology and neurosonogram.

## METHODS

The study was carried out in the department of Paediatrics, Andhra medical college, King George Hospital, Visakhapatnam, Andhra Pradesh, India.

Prospective study of 200 newborns with neonatal seizures who were admitted in NICU King George Hospital, Visakhapatnam, between July 2013 to July 2014.

### *Inclusion criteria*

- Babies included were both term and preterm babies
- Babies in first four wks of life with clinical evidence of seizures

### *Exclusion criteria*

Neonates presenting with jitteriness were excluded from study.

Each case was examined in detail with reference to history, clinical manifestations. A record of physical findings was made and neurological examination was done in each case.

All neonates had basic investigations such as complete blood picture, C reactive protein, blood sugar, chest x-ray and relevant biochemical and microbiological investigations like serum calcium, magnesium, blood for culture and sensitivity, cerebrospinal fluid analysis for proteins, sugar, cell count and type, cerebrospinal fluid for culture and sensitivity, serum electrolytes.

All the details of history, physical examination including the analysis of investigations were entered in a proforma.

Criteria for diagnosing various biochemical disturbances and haematological parameters

- Hypocalcaemia-serum calcium <7.0 mg/dl
- Hypercalcaemia-serum calcium >11 mg/dl
- Hypomagnesaemia-serum magnesium <1.5 mg/dl
- Hypermagnesaemia-serum magnesium >2.5 mg/dl
- Hyponatremia-serum sodium < 130 mg/dl
- Hypernatremia-serum sodium> 150 mg/dl
- Hypokalemia-serum potassium< 3.5 mg/dl
- Hyperkalemia-serum potassium > 5.5 mg/dl
- Hypoglycemia-serum glucose < 40 mg/dl
- Polycythemia-PCV >65.

## RESULTS

The present study is descriptive in nature where clinical spectrum of neonatal seizures in neonates were studied. 1500 neonates were admitted in NICU during the study period, among them 200 (13.3%) developed neonatal seizures.

### *Etiology*

The various etiologies of neonatal seizures and their frequency distribution is shown in Table 1.

**Table 1: Etiology of neonatal seizures.**

| Cause | No. of cases | Percentage |
|---|---|---|
| HIE | 90 | 45% |
| ICH | 28 | 14% |
| Meningitis | 24 | 12% |
| Hypoglycemia | 22 | 11% |
| Hypocalcemia | 8 | 4% |
| Others | 28 | 14% |

Perinatal asphyxia was the most common cause of neonatal seizures. ICH the second most common cause. Among metabolic causes hypoglycaemia was the most common cause of neonatal seizures.

### *Organism*

Of the 200 cases, meningitis accounts for 24 cases. Of these the most common organism causing meningitis is *E.coli* followed by *Klebsiella.* The frequencies are shown in the Table 2.

**Table 2: Distribution of various microorganisms implicated in neonatal seizures.**

| Organism | Percentage |
|---|---|
| *E.coli* | 36% |
| *Klebsiella* | 30% |
| *S.aureus* | 19% |
| GBS | 7% |
| Others | 8% |

Neurosonographic abnormalities

**Table 3: Neurosonogram findings.**

| Neurosonogram findings | Present study |
|---|---|
| Diffuseechoesparenchymal | 55.3% |
| Slit like ventricles | 21% |
| Focalechoesparenchymal | 7.9% |
| Periventricular echoes | 15.8% |

***Outcome of various causes***

Of the total 90 cases of HIE 79 (87.80%) neonates were alive and discharged from the hospital and 11 died (12.20%).

In the present study the total number of neonates with ICH was 28 of which 24 (85.70%) were alive and 4 (14.30%) died. In the present study of the total 24 cases with meningitis 22 (91.70%) babies survived with appropriate antibiotic therapy and 2 (8.30%) babies died. In the present study all the babies with hypoglycaemia i.e., 22 babies (100%) were alive and discharged. In the present study all the cases with hypocalcemia i.e., 8 cases (100%) were alive and discharged. In the present study of the total cases i.e., 28 cases with etiologies other than the above mentioned etiologies 26 babies (92.86%) survived and 2 babies (7.14%) died.

## DISCUSSION

Neonatal seizures typically signal underlying significant neurological disease. The recognition of etiology is often helpful with respect to prognosis and management. Biochemical disturbances and meningitis occur frequently in neonatal seizure either as an underlying cause or as an associated abnormality. In their presence, it is difficult to control seizures and there is risk of further brain damage.

The present study was conducted on neonates with seizures admitted to neonatology unit of King George Hospital, Visakhapatnam during the study period from August 2013 to July 2014.

A total of 1500 neonates were admitted to the neonatology unit during the study period. Out of them 200 neonates had seizures, making an incidence of 13.3% in hospitalized neonates.

A study done by Kumar A et al showed an incidence of 19.2% of neonatal seizures in hospitalized neonates6. Compared to this study the incidence of neonatal seizures in present study is much less, this is probably due to much higher cases of birth asphyxia in their study.

200 neonates had seizures during this study period out of which 116 were males. Several series of neonatal seizures (Keen 1969, Cockburn 1973, Knauss 1977, Holden 1982 and Bergman 1983) showed a male preponderance.

**Table 4: Age at onset of seizures.**

| Age of onset of seizures | Present study | Study by Dr. Sahana and Dr. Anjaiah |
|---|---|---|
| <24 hours | 53% | 51.37% |
| 24-72 hours | 24% | 26.61% |
| >3 days | 23% | 22.02% |

The above table in the present study shows that the incidence of neonatal seizures in the first 24 hours is higher which is consistent with other studies.

In a study done on 100 neonates by Eston et al, HIE accounted for 37%, ICH (7%) meningitis (5%), hypoglycaemia (3%).7 Kumar A et al in their study showed frequency of HIE (67.76%), ICH (11.76%), meningitis (7%), hypoglycaemia (14.3%).[9] Goldberg et al in his ten year review of 81 cases had HIE (16%), ICH (6%), hypoglycaemia (6%) and hypocalcaemia (2%), meningitis (8%) remaining were due to congenital abnormalities.[8]

Nelson et al in year 2006 reported that up to 60% of neonatal seizures were due to hypoxic ischemic encephalopathy and most of cases occurred in first 24 hours of life.[9] Ronnen et al showed HIE (405), ICH (15%), meningitis (20%) and hypoglycaemia (3%).[10] Aierde 41 studied 57 infants from Nigeria. The distribution in his study was HIE (47.4%), meningitis (9%), hypoglycaemia (11.3%) and hypocalcaemia (6%). Andre et al in their study had frequency of HIE (49%), ICH (14%), meningitis (2%), hypoglycaemia (1%).[11] Lien et al in their study of 40 neonates showed a frequency HIE (37%), ICH (12%), meningitis (5%).[12]

In present study of 200 neonates majority of neonates with seizures had HIE 90(45%) followed by ICH 28 (14%), meningitis 24 (12%) and biochemical abnormalities hypoglycaemia 22 (11%), hypocalcaemia 8 (4%) and other causes 28 (14%) which is consistent with other studies. HIE is most common cause of neonatal seizures in present study which is consistent with the other studies. The most common biochemical abnormalities in present study are hypoglycaemia, hypocalcaemia which are consistent with other studies. Rose LA et al studied full born infants with seizures and hypoglycaemia was observed in 7 (3.1%) of cases, 1 case developed seizures on day 1, 3 cases on day 2, 2 cases on day 3, 1 case in between days 4 to 7 and no case after that.[13] Keen et al studied 100 cases of neonatal seizures and observed that hypoglycaemia alone was present in 6 cases.[14] Aierde et al found that hypoglycaemia was responsible for seizure in 11 neonates (19.3%) out of total 57 studied by him prospectively.[6] Kumar A et al found 5 cases of primary hypoglycaemia (14.3%) in their series of 35 cases of neonatal seizures studied.[9] Hypoglycemia was present in 4 (2.5%) cases of birth asphyxia, 1 case of

meningitis and in one case of septicaemia having neonatal seizures.

Infection of central nervous system is an important cause of neonatal seizure. Rose LA et al studied 137 neonates and found that 13 (9.5%) of cases were due to infection.[13] An incidence of 5% was quoted by Goldberg HJ et al.[8] His observations were based upon an analysis of 235 cases of neonatal seizures over a period of 10 years. In all, he found 11 cases of neonatal seizures due to meningitis and one case due to intra uterine cytomegalovirus infection. According to Nelson et al in 10-20% of cases of neonatal seizures, infection was the underlying etiology and usually occurred after third day of life. Airede et al found that out of 57 cases due to neonatal seizures infection was etiological factor in 7 cases i.e. 8.8%.[15] In present study, meningitis accounted for 12% of cases, which is consistent with the findings of other studies.

In study done by Sood A et al the most common organisms implicated were *E. coli* (45%), *Klebsiella* (42%), group B *Streptococci* (6%), and Staph. Aureus (4%) and others (3%).[16] Bergman et al reported the frequency was *E. coli* (38%), *Klebsiella* (28%), staph aureus (25%), *Streptococci agalactiae* (5%) others (4%).[17] Ortibus EL et al in his study of 81 neonates reported frequency of *E. coli* (29%), *Klebsiella* (35%), Staph. *Aureus* (26%), *Streptococci agalactiae* (4%), others (6%).[18]

The present study showed *Escherichia coli* (36%), *Klebsiella* (30%), *Staphylococcus aureus* (19%), Group B Streptococci (S. agalactiae) (7%), others (8%) which is consistent with the other studies.

Neurosonogram was done in all the cases of which 38 cases had abnormalities. The rest had normal neurosonogram. Diffuse parenchymal echoes were the most common finding.

**Table 5: Study of neurosonogram abnormality in neonates with HIE.**

| | Present study | N. K. Anand and A. K. Gupta et al |
|---|---|---|
| Diffuse parenchymal echoes | 55.3% | 53% |
| Slit like ventricles | 21% | 20% |
| Focal parenchymal echoes | 7.9% | 6% |
| Periventricular echoes | 15.8% | 21% |

80% of the cases with normal neurosonogram were found to be normal on follow up. 38 cases with abnormal neurosonogram were followed up. Out of 21 cases with diffuse parenchymal echoes 17 cases developed development delay. 5 cases out of 8 cases with slit like ventricles developed development delay.

## CONCLUSION

In the present study 200 babies with neonatal seizures were studied. 53% of seizures occurred in the first 24hrs of life Etiology in majority of the cases of neonatal seizures was hypoxic ischemic encephalopathy (45%) followed in frequency by intracranial haemorrhage (14%), meningitis (12%), hypoglycaemia (11%), hypocalcemia (4%) and others (14%). Biochemical changes accounted for 18% of the neonatal seizures.Most common biochemical abnormalities noted were hypoglycaemia, hypocalcemia and hyponatremia. Meningitis accounted for 12% of neonatal seizures. The most common organism implicated in neonatal seizures was *Escherichia coli* (36%), followed by *Klebsiella* (30%), *Staphylococcus aureus* (19%), *Streptococci agalactiae* (7%) and unknown (8%). Gram negative organisms accounted for most of the cases of neonatal seizures with meningitis. Biochemical abnormalities are common in neonatal seizures. Biochemical abnormalities which could account for seizures were seen in 18% of the

cases. Hypoglycaemia, hypocalcemia and hyponatremia are the most common biochemical abnormalities. These abnormalities may significantly contribute to seizure activity and possibly correction of these abnormalities may play a significant role in seizure control. A biochemical workup is necessary for all cases of neonatal seizures. Meningitis was seen in 12% of the cases and most common organism isolated from cerebro spinal fluid was *Escherechia coli.* Appropriate treatment with antibiotics is essential. Examination of cerebrospinal fluid is essential workup in cases of neonatal seizures. 80% of the cases with normal neurosonogram were found to be normal on follow up. Significant number of cases with diffuse parenchymal echoes on follow up were found to be abnormal. Cases with perinatal asphyxia and intraventricular hemorrhage had poor outcome. Neurosonogram had good potential in predicting neurological outcome in neonates with perinatal asphyxia. Neurosonogram should be incorporated in the routine evaluation of seizures. Abnormal neuroimaging and EEG were good predictors for the outcome and developmental delay.

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