

## Research Article

# Biochemical and microbiological evaluation of neonatal seizures

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### ABSTRACT

**Background:** Neonatal seizure is a common neurological problem in the neonatal period. Neonatal seizures have always been a topic of interest because of their universal occurrence. A varied number of conditions are capable of causing seizures in the neonatal period. The highest incidence of neonatal seizure occurs during first 24 hours of life. The aim was to study biochemical and microbiological factors related with neonatal seizures.

**Methods:** The present study was conducted in the neonatology unit, department of pediatrics, SVS hospital and medical college. The study was done to assess the biochemical changes and microbiological organisms implicated in neonatal seizures.

**Results:** In the present study, out of 1080 babies admitted to neonatology unit during the study period 100 developed seizures giving a hospital incidence of 9.25%. Etiology in majority of cases of neonatal seizures was hypoxic ischemic encephalopathy (43%). Biochemical changes accounted for 17% of neonatal seizures. Meningitis accounted for 11% of neonatal seizures. The most common organism implicated in neonatal seizures was *Escherichia coli* (35%).

**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.

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

### INTRODUCTION

Neonatal seizure is a common neurological problem in the neonatal period. Neonatal seizures have always been a topic of interest because of their universal occurrence. A varied number of conditions are capable of causing seizures in the neonatal period. The highest incidence of neonatal seizure occurs during first 24 hours of life.<sup>1</sup>

In 1870, Hughlings Jackson described a seizure as an 'excessive discharge of nerve tissue on muscle' today this definition is expanded to include effects of sensory and autonomic nervous systems, including paroxysmal alterations in behavioural state. All those who care for the

newborn need a working knowledge of the likely causes and a management plan for this important emergency. Prompt diagnosis, investigation and treatment are vital as delayed recognition of a treatable cause can have a significant impact on the child's subsequent neurological outcome.<sup>2</sup>

Neonatal seizures often signal an underlying ominous neurological condition, most commonly hypoxic-ischemia. The other common etiologies of neonatal seizures are intra-ventricular hemorrhage or intra-parenchymal hemorrhage, meningitis, sepsis or metabolic disorders.<sup>3</sup>

There is increasing evidence that neonatal seizures have an adverse effect on neuro-developmental outcome and predispose to cognitive, behavioural or epileptic complications in later life.<sup>1</sup>

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 known as kindling.<sup>4</sup>

Seizures are the most distinctive manifestation of significant CNS disease in the newborn. Seizures are more common in the newborn period than at any other time in life, and that the tendency toward recurrent seizures and status epilepticus is far greater in the newborn. Neonates are at particular risk for the development of seizures because metabolic, toxic, structural, and infectious diseases are more likely to be manifested during this time than at any other period of life.<sup>3</sup>

The international classification of epileptic seizures does not apply to newborn seizures because neonates are unstable to sustain organized discharges and do not manifest generalized tonic clonic seizures. Any abnormal, repetitive and stereotypic behaviour in neonates should be evaluated as possible seizure.<sup>5</sup>

The presence of a 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.<sup>6</sup>

Biochemical disturbances occur frequently in neonatal seizures either as underlying causes or as an associated abnormality. In their presence it is difficult to control seizure and there is a risk of further brain damage. Early recognition and treatment of biochemical disturbances are essential for the optimal management and satisfactory outcome.<sup>7</sup> Meningitis is most important cause of neonatal seizures. Prompt recognition and treatment is essential to avoid the sequelae.<sup>1</sup> Hence the present study was carried out to study biochemical and microbiological factors related with neonatal seizures.

## METHODS

The hospital is a teaching institute situated in district headquarters with 750 beds, which includes level I NICU with 12 capacity and level II with 6 capacities. A total of 1080 cases admitted to the NICU during the study period. 100 neonates with seizures during the period Jan 2009-Aug 2010 have been selected for study.

### Inclusion criteria

- All the neonates with clinical evidence of seizures were selected for study.

### 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 < 3.5mg/dl
- Hyperkalemia-serum potassium > 5.5 mg/dl
- Hypoglycemia-serum glucose < 40 mg/dl
- Polycythemia-PCV >65

## RESULTS

Present study was conducted in the department of paediatrics, neonatology unit, S.V.S hospital and medical college from January 2009 to August 2010.

**Table 1: Distribution of neonates with seizures as per etiology.**

Cause	No. of cases	Percentage
Hypoxic ischemic encephalopathy (HIE)	43	43%
Intra cerebral hemorrhage (ICH)	16	16%
Meningitis	11	11%
Hypoglycaemia	9	9%
Hypocalcaemia	5	5%
Hyponatremia	3	3%
Unknown	13	13%

Total number of neonatal admissions during the study period was 1080. A total of 100 neonates with neonatal seizures who fulfilled the inclusion criteria were included in the study. The most common cause of neonatal

seizures was found to be HIE in 43% of cases followed by ICH in 16% of cases. The most common organism implicated in neonatal seizures was *Escherichia coli* (35%) followed in frequency by *Klebsiella* (30%), *Staphylococcus aureus* (20%), *Streptococci agalactiae* (3%), unknown (12%).

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

Organism	Percentage (%)
<i>E. coli</i>	35%
<i>Klebsiella</i>	30%
<i>Staphylococcus aureus</i>	20%
Group B streptococci	7%
Others	8%

In comparison to Estan et al, it was found that 43% of cases of neonatal seizures are due to HIE. They found it as 49%. It was also found that ICH was responsible for 16% of cases compared to 7% by them.

**Table 3: Comparison of present study with Estan et al 1997.<sup>8</sup>**

Cause	Present study (%)	Estan et al <sup>8</sup> (%)
Hypoxic ischemic encephalopathy (HIE)	43	49
Intra cerebral hemorrhage (ICH)	16	7
Meningitis	11	5
Hypoglycaemia	9	3
Hypocalcaemia	5	0

## 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. This prospective study was conducted on neonates with seizures admitted to neonatology unit of SVS hospital and medical college during the study period from January 2009 to August 2010. A total of 1080 neonates were admitted to the neonatology unit during the study period. Out of them 100 neonates had seizures, making an incidence of 9.25% in hospitalized neonates.

A study done by Kumar A et al showed an incidence of 19.2% of neonatal seizures in hospitalized neonates.<sup>9</sup> 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.

In a study done on 100 neonates by Eston et al, HIE accounted for 37%, ICH (7%) meningitis (5%), hypoglycaemia (3%).<sup>8</sup> Kumar A et al in their study showed frequency of HIE (67.76%), ICH (11.76%), meningitis (7%), hypoglycaemia (14.3%).<sup>9</sup> 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.<sup>10</sup>

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.<sup>6</sup> Ronnen et al showed HIE (40%), ICH (15%), meningitis (20%) and hypoglycaemia (3%).<sup>11</sup> 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%).<sup>13</sup> Lien et al in their study of 40 neonates showed a frequency HIE (37%), ICH (12%), meningitis (5%).<sup>14</sup>

In present study of 100 neonates majority of neonates with seizures had HIE (43%) followed by ICH (16%), meningitis (11%) and biochemical abnormalities hypoglycaemia (9%), hypocalcaemia (5%) and hyponatremia (3%) 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 and hyponatremia 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.<sup>15</sup> Keen et al studied 100 cases of neonatal seizures and observed that hypoglycaemia alone was present in 6 cases.<sup>16</sup> Aierde et al found that hypoglycaemia was responsible for seizure in 11 neonates (19.3%) out of total 57 studied by him prospectively.<sup>11</sup> Kumar A et al found 5 cases of primary hypoglycaemia (14.3%) in their series of 35 cases of neonatal seizures studied in 1995.<sup>9</sup> Hypoglycemia was present in 4 (2.5%) cases of birth asphyxia, 1 case of meningitis and in one case of septicaemia having neonatal seizures.

Hypoglycemia was more in study by Kumar A et al (14.3%).<sup>9</sup> This was probably due to late referrals from outside centres and delayed feeding in their study. In present study hypoglycaemia was present in 9% of cases which is consistent with the other studies. Dodd K et al reported thirty three instances of hypocalcaemia in the newborn period from children hospital of Cincinnati from 1937 to 1947, 48 cases presented with convulsions, vomiting, and edema.<sup>17</sup> 24 cases with possible sign of

hypocalcaemia were found. In infants apparent tetany the serum calcium varied between 6 and 9 mg. Rose et al studied 137 full term babies with convulsions.<sup>15</sup> 28 cases (20.4%) were due to hypocalcaemia. In 3 cases convulsions occurred on day 1 in 3 cases on day 2, in 1 case on day 3, in 13 cases on 4-7 days, in 6 cases on 8-15 days and in 2 cases after 15 days.

Tsang CR et al reported that 12 out of 33 (37.36%) premature infants had serum calcium less than 7 mg per 100 ml.<sup>18</sup> Nelson et al in 2006 observed that 10-20% of cases were due to hypocalcaemia and hypomagnesaemia.<sup>6</sup>

Aierde et al studied 57 infants with neonatal seizures admitted to the special care baby unit of Jos University teaching hospital, Nigeria over a 3 year period and observed that hypocalcaemia was responsible cause in 5 (8.9%) of cases.<sup>12</sup> 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.<sup>15</sup> An incidence of 5% was quoted by Goldberg HJ et al.<sup>10</sup> 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.<sup>6</sup> Airede et al found that out of 57 cases due to neonatal seizures infection was etiological factor in 7 cases i.e. 8.8%.<sup>12</sup> In present study, meningitis accounted for 11% 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%).<sup>19</sup> Bergman et al reported the frequency was *E. coli* (38%), *Klebsiella* (28%), *staph aureus* (25%), *streptococci agalactiae* (5%) others (4%).<sup>20</sup> 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%).<sup>21</sup>

The present study showed *Escherichia coli* (35%), *Klebsiella* (30%), *Staphylococcus aureus* (20%), Group B *Streptococci* (*S. agalactiae*) (7%), others (8%) which is consistent with the other studies.

## CONCLUSION

Most common biochemical abnormalities noted were hypoglycaemia, hypocalcaemia and hyponatremia. 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. Meningitis was seen in 11% of cases and common organism isolated from cerebrospinal fluid

was *Escherichia coli*. Appropriate treatment with antibiotics is essential. Examination of cerebrospinal fluid is essential work up in cases of neonatal seizures.

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