Original Article

# A study of clinical profile of neonatal seizures

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## Abstract

**Objective:** To study the clinical profile of neonatal seizures. **Design:** Prospective observational study. **Settings:** Neonatology Intensive Care Unit at tertiary care hospital. **Outcome Measures:** Association of risk factors like preconceptional, postconceptional, antepartum, intrapartumand neonatal with neonatal seizures and their outcome. **Results:** 132 neonates with observed neonatal seizures were studies Gestational age group of more than 37 weeks and birth weight more than 2500 gms had highest frequency of seizures 62.1% and 45.4% respectively. Meconium stained liquor was the most frequent perinatal risk factor followed by prematurity, prolonged labour, foetal distress, premature rupture of membranes and preeclampsia. Seizures occurred with increased frequency in between 24 hours to 7 days, most of them being subtle. The most common metabolic abnormality was found to be hypoglycaemia. Birth asphyxia accounted for 61(46.2%) cases of seizures either alone or in combination with other etiologies. **Conclusion:** We conclude that having the knowledge of these factors will help in anticipation of seizures in presence of perinatal risk factors and careful monitoring for occurrence of seizures in babies and proper early treatment. This will also help in reducing neonatal mortality.

**Keywords:** Neonatal Seizures, risk factors, clinical profile.

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## INTRODUCTION

A newborn with a seizure represents a fairly common emergency in an NICU. Even with recent new advances in perinatal care and fetal monitoring, the burden due to neonatal seizures remains high as mortality has decreased and morbidity has increased due to better neonatal care. Neonatal seizures are suggestive of neurological dysfunction. The most common seizures type in neonatal are focal or multifocal clonic, tonic, myoclonic, and subtle[1].The subtle seizures comprises variety of motor and autonomic phenomena. No racial preponderance is known and the sex-based frequency differences have not been described. The main causes of neonatal seizures are perinatal asphyxia, metabolic abnormalities (hypoglycemia, hypocalcaemia, hypomagnesaemia, pyridoxine deficiency, hyponatremia and hypernatremia, and Kernicterus), infection (sepsis, meningitis and encephalitis), bleeding (subarachnoid, subdural, thrombosis and Intraventricular hemorrhage),developmental anomalies (cerebral dysgenesis and incontinentia pigmenti), and other causes (drug withdrawal, hyperthermia, benign familial neonatal seizures, benign idiopathic neonatal seizures and benign sleep myoclonus)[1,2]. Other causes like inborn errors of metabolism, although a rare cause of neonatal seizures, are extremely important to consider as their detection allows appropriate genetic counselling and may permits pecifictherapy[3]. The causes of seizures in preterm neonates are different from that seen in term neonates, where the HIE is the most frequent cause in term neonates, followed by cerebral malformations and metabolic disturbances, while in preterm neonates intra ventricular hemorrhage and infections are the most frequent causes.[4] Neonates with seizures are at risk of death, whereas survivors are at a increased risk of neurological sequelae, developmental delay, later epilepsy and cognitive impairment so, we need to initiate an early diagnostic workup to determine the causes, depending upon the facilities available[5]. Prognosis of the neonate is mainly determined by the aetiology[6]. The prognosis after hypocalcemic seizures and in familial neonatal seizures is excellent. Symptomatic hypoglycaemia and meningitis have a 50% chance of sequelae in the survivors. In hypoxic ischaemic

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encephalopathy the prognosis depends on the grade (overall30-50% normal), while CNS malformations are generally associated with poor outcome. Very low birth weight infants with clinical seizures have a higher incidence of impairment than preterm infants without seizures. Despite its clinical significance and incidence, there are number of problems in diagnosis and management. The primary strategy for effective management is to estimate overall incidence and etiology of neonatal seizures with reference to each population so that high index of suspicion can be maintained. The purpose of the current study was to determine incidence, etiology and outcome of neonatal seizures so that it will be a helpful tool for management.

## MATERIALS AND METHODS

This prospective descriptive study was conducted in Neonatal Intensive care unit from 1st January 2014 to 30th June 2015. All cases of witnessed neonatal seizures with gestation age more than 28 weeks and weight more than 1 kg admitted in NICU before 28 days of life were enrolled in this study. Procedure was explained to the parents and informed oral and written consent was taken. Study protocol was approved by institutional ethical committee. A detailed antenatal, intranatal and postnatal history was taken in a pre designed proforma with special emphasis on gestational age, parity, history of maternal illness during pregnancy, birth events which included perinatal risk factors, mode of delivery, birth asphyxia and resuscitation required. Baseline characteristics of the convulsive neonate were recorded at admission which included sex of neonate, gestational age of neonate as assessed by using modified Ballard scoring system, birth weight, head circumference and length. All babies with seizures were examined at admission with detailed examination of central nervous system. Clinical details of the witnessed seizure episode was noted which included the age in days of neonate at the time of first seizure ( less than 24 hours, 24 hours to 7 days and after 7 days of life) and type of seizure. The neonatal seizures were classified as per Volpe's classification into subtle, multifocal tonic, focal clonic, focal tonic and myoclonic. The blood samples of all neonates included in the study were sent for the following first line investigations: Complete blood counts, blood glucose level at the time of convulsion, serum electrolytes- serum sodium, serum potassium and serum calcium, CRP, blood culture and sensitivity, cranial ultrasound. Blood samples were taken immediately after seizures and before institution of any specific treatment. An ultrasound was done in all neonates with seizures. Second line of investigations was done in selected few cases as and when indicated - cerebral spinal fluid analysis, CT scan, MRI, serum magnesium, IEM screen (serum ammonia, ABG, urine ketones), EEG, Serum bilirubin. Cerebral spinal fluid analysis was carried out in selected cases whenever indicated to find out the etiology of seizures and in all cases where CRP was positive. Serum bilirubin level was done in neonates where risk factors like RH incompatibility and clinical findings suggestive of its etiology in seizure were present. IEM screening was done in suspected cases with persistent hypoglycemia or relevant history like bad obstetric history. All neonates were managed as per the standard protocol of NICU with all aseptic care. A detailed course in NICU was noted and short term outcome of each neonate was noted in terms of morbidity and mortality as death or complete recovery or having neurological sequelae. Sequelae were noted by assessment of tone of the baby, number of anticonvulsants on discharge and significant ultrasonographic findings. The data was collected on proforma and analysed using descriptive statistics. The statistical software namely SPSS 21.0 were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs and tables etc.

## RESULTS

132 cases of witnessed neonatal seizures admitted in NICU constituted the material of the study. Males were affected more in this study than females. Among the 132 neonates, 60 (45.4%) babies had weight more than 2.5 kg, 38 babies (28.8%) had weight between 1.5 to 2.5 kg and 34 babies (25.7%) had weight less than 1.5kg. In this study, maximum babies had weight more than 2.5 kg. 82 babies (62.1%) had gestational age more than 37 weeks, 45 babies (34.1%) with gestational age between 30-37weeks and 5 babies (3.8%) with gestational age between 28-30 weeks. 84 babies(63.6%) were born to primiparous mothers and 48 babies (36.4%) were born to multiparous mothers. meconium stained liquor- 27 (20.4%) was the most frequent perinatal risk factor followed by prematurity- 19 (14.4%) and prolonged labour-19 (14.4%).Foetal distress was associated with 17 cases (12.9%), premature rupture of membranes- 14 (10.6%) and preeclampsia with 10 cases (7.7%). Intrauterine growth retardation was associated with 8 cases (6%). Rh incompatibility was seen with 6 cases (4.6%), gestational Diabetes mellitus was seen in 3 cases (2.2%) and bad obstetric history was present in 1 case (0.8%).There were 8 cases (6%) of neonatal seizures with no associated perinatal risk factors. Among the 132 babies, 84 (63.6%) of the babies were delivered by normal vaginal delivery and 48 (36.4%) babies were born by assisted delivery either LSCS, ventouse or forceps. Out of 48 assisted deliveries, 35 babies were delivered by Caesarean section, 9 babies by forceps and 4 by ventouse.

Hence maximum babies in this study were delivered by normal vaginal delivery. 48 babies (36.4 %) had the first convulsion in less than 24 hours, 78 babies (59.1%) had between 24 hours and 7 days and 6 babies (4.5%) had convulsion after 7 days. Maximum babies in this study developed convulsions between 24 hours to 7 days. Overall, subtle seizures were the most common seizure type found in 53(40.1%) neonates followed by focal clonic seizure type found in 32(24.2%) neonates and focal tonic in 30 (22.8%) neonates. In preterm babies, generalised tonic seizures were the commonest type of seizures- 13 (76.5%), and in term babies, focal Clonic was the commonest type of seizure 28 (87.5%). None of the cases had myoclonic seizures. Out of 132 cases of neonatal seizures studied, only 58 cases were associated with metabolic disturbances. 49 cases (84.4 %) had hypoglycemia, 7 cases (12 %) had hypocalcemia, and 1 case each (1.8 %) of hypomagnesemia and hyponatremia. The most common metabolic abnormality in this study was found to be hypoglycaemia.

**Table 1:** Shows the distribution of cases according to multifactorial etiology

| Etiology | No. of cases (n=132) | Percentage (%) |
|---|---|---|
| Birth asphyxia | 35 | 26.5 |
| Birth asphyxia with sepsis | 16 | 12.1 |
| Birth asphyxia with hypoglycaemia | 6 | 4.5 |
| Birth asphyxia with hypocalcemia | 2 | 1.5 |
| Birth asphyxia with sepsis with hypoglycaemia | 2 | 1.5 |
| Sepsis | 11 | 8.3 |
| Sepsis with meningitis with hypoglycaemia | 10 | 7.5 |
| Sepsis with hypoglycaemia | 3 | 2.2 |
| Sepsis with IVH with hypoglycaemia | 4 | 3 |
| Sepsis with kernicterus with hypoglycaemia | 4 | 3 |
| Sepsis with meningitis with hypoglycaemia with Hyponatremia | 1 | 0.8 |
| Sepsis with hydrocephalus | 1 | 0.8 |
| IVH | 10 | 7.8 |
| Symptomatic hypoglycemia | 16 | 12.1 |
| Kernicterus | 4 | 3 |
| Hypocalcemia | 5 | 3.8 |
| Hypomagnesemia | 1 | 0.8 |
| Pyridoxine dependent seizures | 1 | 0.8 |
| **Total** | **132** | **100** |

Birth asphyxia accounted for 61 (46.2%) cases of seizures either alone or in combination with other etiologies. Isolated HIE was seen in 35 (26.5%) cases and associated with sepsis in16 cases (12.1%) cases. Among the metabolic abnormalities associated with birth asphyxia, hypoglycemia was the most common in 6 (4.5%) cases followed by hypocalcemia- 2 (1.5%) cases. There were 2 cases associated with sepsis and hypoglycemia (1.5 %). Sepsis accounts for total 32 cases and 18 cases as above were associated with birth asphyxia and hypoglycemia. Isolated sepsis accounts for 11 cases (8.3%), associated with meningitis and hypoglycemia in 10 cases (7.5%) and with only hypoglycemia in 3 cases (2.2 %). Intraventricular hemorrhage along with sepsis and hypoglycemia accounts for 4 cases (3%). Sepsis associated with kernicterus and hypoglycemia was found in 4 cases (3%). There was one case of sepsis associated with hydrocephalus (0.8 %) which was further diagnosed as Toxoplasmosis. Metabolic abnormalities like hypoglycemia, hypoclcaemia –5 (3.8%) and hyponatremia-1( 0.8%) and hypomagnesemia -1 ( 0.8%) accounts for 58 cases but hypoglycemia was the only primary metabolic abnormality in only 16 cases ( 12.1%) causing neonatal seizures in the current study. Hypoglycemia was associated with HIE, sepsis and intracranial haemorrhage (ICH).Hyponatremia was seen in one case (0.9%) associated with sepsis and meningitis and hypoglycaemia. There was one case of pyridoxine dependent seizure in this study (0.9%) Isolated kernicterus accounted for 4 cases (3%) and isolated intraventricular haemorrhage accounted for 10 cases (3%).

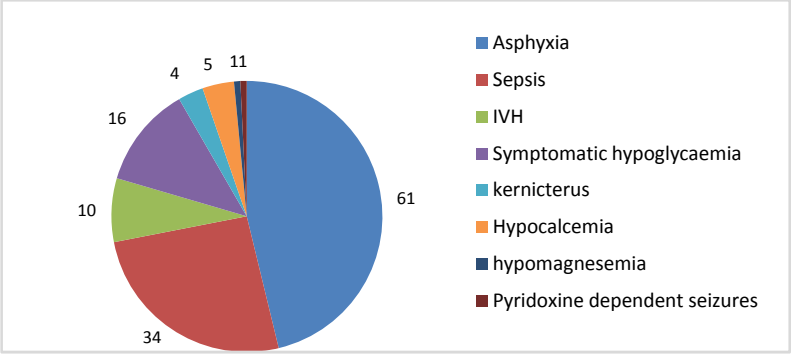


**Figure 1:** Shows the distribution of cases according to multifactorial etiology (n=132)

## DISCUSSION

Neonatal seizures with its high mortality and morbidity rates still remains a diagnostic and treatment challenge for neonatal health care providers. Given the numerous advances which have occurred in the care of the newborns, it is surprising that so much controversy still surrounds the definition, significance, detection and management of neonatal seizures. Paradoxically, technological developments in the form of bedside monitoring have exacerbated rather than eased the problem by facilitating diagnosis of subclinical and subtle convulsions and advances in neonatal care have increased the morbidity due to neonatal seizures mainly due to increased survival of premature babies. The uppermost concern in both parents and pediatrician's mind is the long term neurological outcome in a baby with neonatal seizures. For many decades, it has been clear that the etiology of neonatal seizures is one factor critical in determining outcome. Newborns with transient correctible metabolic abnormalities, focal ischemia do well, as opposed to those with hypoxic-ischemic encephalopathy (HIE), CNS infections and hemorrhage. It is also difficult to separate out the impact of the etiology from the impact of seizures themselves on the immature developing nervous system. In the present study, incidence of neonatal seizures was 6.43% of the total admitted neonates in NICU in the study period. In a study by Sahana *et al*[7], incidence was found to be 8.38% with incidence in hospital deliveries 7.04% and the incidence for outside deliveries is 14%. This difference was explained by better availability of facilities in hospital deliveries. In a study by Alyasiri *et al*[8], the incidence of neonatal seizures was 3.9%. This low incidence was explained by the fact their study was conducted in a neonatal care unit and not in an intensive care unit. Male babies were more than female babies in the present study showing a ratio of 1.3:1. These results are comparable with observations by other authors. Male preponderance in the neonatal seizures may be linked to the X-linked immunoregulatory gene resulting in hosts' susceptibility. In the present study the higher proportion of cases were with birth weight more than 2.5 kg. The results of other studies also showed increased proportion of cases with birth weight more than 2.5 kg. However, Kohel *et al* [9] and Saliba *et al* [10] in their population based studies reported increased incidence of seizures with decreasing birth weight. This effect is probably related to prematurity. In this study, seizures were found to be more common in neonates with gestational age more than 37 weeks. This was also seen in studies by Suryavanshi *et al*[11], Malik *et al*[12]. However similar to birth weight Kohelet *et al* and Saliba *et al* in their population based studies reported increased incidence of seizures with decreasing gestational age. The incidence appears to be less in premature babies in this study because majority of seizures in preterms are subtle. EEG is required for proper recording of neonatal seizures particularly in preterms. Since all the neonatal seizures are recorded only by clinical observation the disparity is seen in this study. As compared to multiparous mothers, seizures were observed more in primiparous mothers in this study. Similar results were observed by Sahana *et al*[7] and Suryavanshi *et al*[11]. This may be explained by the problems of prolonged labour, feeding difficulties leading to delayed feeding seen in primiparity. In the present study, Meconium stained liquor as a risk factor was observed in 20% of the cases, which is comparable to study by Rajput *et al*[13]. Prolonged labour as a risk factor was seen in 14.4% of cases of neonatal seizures and comparable results were seen by Suryavanshi *et al*[11]. PROM as a risk factor was observed in 14% of the cases in the present study. Similar results were seen by Suryavanshi *et al*[11].The variations in the occurrence of perinatal risk factors probably reflect differences in the rates of occurrence of the predisposing risk factors in the various studies. In the present study, more cases of neonatal seizures were observed between 24 hrs to 7 days of age of the baby as compared to the first 24 hours. Similar result was seen by Suryavanshi *et al*[11] and Sahana *et al*[7]. Onset of neonatal convulsions was seen maximum in first one week of life in almost 95% of cases in this study. Seizure percentage decreases as day of onset

increases. This has been found true in almost all of the studies as birth asphyxia is the commonest cause of neonatal seizures found globally and most seizures in the asphyxiated new born occur in the first 72 hours of life. Sahana *et al*[5] reported that 4 (3.7%) babies had convulsions after 7 days, which were due to septicemia. In our study, 6 babies had convulsions after 7days of life, 2 of them had intraventricular hemorrhage and 4 had multifactorial etiology mainly septicemia. In this study seizures are classified into 5 types-subtle, focal clonic, focal tonic, generalised tonic and myoclonic.[14] In this study,the most common type of seizure was subtle -53 (40.1%), followed by focal clonic- 32 (24.2%),focal tonic- 30(22.8%) and generalised tonic- 17(12.9%). There was no observed case of myoclonic seizure in this study. However in different studies, the seizures are classified in varied ways. Subtle seizures were also found the predominant type of seizures by Alyasiri *et al*[8], who had classified them into subtle, tonic, clonic and myoclonic. Also, in a study by Suryavanshi *et al*[11], seizures were classified as subtle, focal clonic, multi-focal clonic, tonic and myoclonic. They also found that subtle seizures were the most common type. Marzoki *et al*[15] classified seizures as subtle, tonic, multi-focal clonic, generalized tonic clonic, focal clonic and unknown cause. In this study, focal clonic was the most common type of convulsion in term babies and generalised tonic convulsions were the most common in preterms. In this study, metabolic causes like hypoglycemia-16 (12.1%), hypocalcemia-5 (3.8%) and hypomagnesemia-1 (0.8%) were the etiology of convulsions. However metabolic disturbances were present in total 58 cases along with other etiologies like birth asphyxia, intracranial bleeding, sepsis and meningitis. Hypoglycemia was present in 49 cases with other causes like sepsis, meningitis, IVH and birth asphyxia. Similar hypocalcemia was seen in 7 cases along with other causes. Similar results of hypoglycemia were reported by studies done by Sahana *et al*[7] and Alyasiri *et al*[8]. Similar results of hypocalcemia were seen by Sahana *et al*[7]. Marzoki *et al*[15] had reported increased cases of metabolic disturbances in their study (47.7%) and this was the main eitiology of seizures in their study. In the literature search of the studies on etiology of neonatal seizures, single etiology was implicated as the cause of seizure in maximum number of studies like Suryavanshi *et al*, Sahana *et al*, Malik *et al*[12], Rajput *et al*[13]. However in the present study, it was observed that as many as 49 cases (37%) had multifactorial etiology. Isolated birth asphyxia was seen in 35 cases whereas birth asphyxia was seen in 26 more cases along with other etiology. Hence in total, birth asphyxia was seen in 46% cases. Similarly, isolated sepsis is seen in only 11 cases but along with other etiologies, it was seen in more 23 cases. Hence sepsis as an etiology was responsible for 23% of the cases. Birth asphyxia was the commonest cause of seizures observed in our study (46%) both isolated and in addition to other etiologies followed by sepsis, metabolic disturbances followed by intraventricular haemorrhage. Suryavanshi *et al*[11] and Malik *et al* [12] reported that birth asphyxia as an etiology of seizure was seen in 46.25% and 53.7% cases respectively which are comparable with the results of our study. Sepsis alone or in addition to other etiologies caused 23% of the cases. Lesser percentage of sepsis was seen in other studies. Alyasiri *et al*[8] and Sahana *et al*[7] reported sepsis as one of the major and preventable etiology of neonatal seizures. In our study, intracranial haemorrhage was seen in 10 (7.8%) cases. Alyasiri *et al*[8] reported intracranial bleed in 10.7% of the cases which is comparable with our study. The incidence of IVH was higher in preterm babies than term babies in our study. Alyasiri *et al* and Suryavanshi *et al* also reported higher incidence of IVH in preterm neonates. In the present study, isolated cases with metabolic abnormalities like hypoglycemia, hypocalcemia, hypomagnesemia and hyponatremia accounted for 16.7% of the cases. Biochemical abnormalities like low glucose and calcium levels were seen in many cases of sepsis, birth asphyxia, intraventricular hemorrhage, but these are also probably effect of the main etiology. In total metabolic abnormalities were present in 24.2% cases along with other co-morbidities. In a study conducted in Nepal by Shah *et al*[16] hypoglycemia and hypocalcemia are the most common biochemical abnormality seen in neonates with seizures and carry a good short term outcome. Number of cases of kernicterus in our study is comparable to that in other studies. This is a preventable cause of seizures and incidence can be decreased by prompt diagnosis and treatment of hyperbilirubinemia. In the present study, 56.8% of the cases were discharge with normal neurological examination whereas 6.8% died and 36.4% had some neurological sequelae. Similar results were found by Alyasiri *et al*[8] in which 56.6% of the babies were discharged and 26% had sequelae. In the present study, maximum number of death were due to birth asphyxia - 6 (66.7%) followed by 3 (33.3%) due to sepsis and related complications. There were no deaths due to intraventricular hemorrhage where 90% of the cases had sequelae on discharge and only 1 was discharged with complete normal neurological examination on discharge. However, the true relation between etiological factors and outcome cannot be commented on during this study as the duration of the study is short and only the immediate outcome at discharge was taken into account and long term follow-up study was not performed.

## CONCLUSION

Neonatal seizures are a leading cause of mortality and morbidity among the neonates in our country. Early recognition and prompt treatment will help in reducing the mortality and morbidity and long term neurological problems in neonates.

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