Original Article

Neonatal seizures: our experience of incidence, etiology and outcome in a tertiary care centre

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Received – 22 April 2014 Initial Review – 20 May 2014 Published Online – 06 July 2014

Abstract

Context: Neonatal seizures often evoke a sense of urgency among physician in charge of newborn as they often indicate a CNS dysfunction. Incidence of neonatal seizures remains high in our community even in this era of advanced perinatal care. Early detection of seizure and its etiology help us to provide specific therapy. **Objectives:** The purpose of this study was to determine the incidence, etiology and outcome of neonatal seizures. **Settings and design:** Prospective hospital based descriptive study conducted in the neonatal unit of tertiary care hospital. **Material and methods:** Consecutive newborns admitted with seizures were included in this study. Data were collected regarding relevant history and examination, thoroughly evaluated for etiology and outcome was documented. Analysed by descriptive statistics and conclusions were drawn. **Results:** One hundred and eight newborns with seizures were included during study period and incidence of neonatal seizure was 5.5%. Hypoxic ischemic encephalopathy (HIE) and sepsis constituted the most common etiologies. HIE was the most common etiology associated with mortality. Abnormal EEG with supressed background activity was present in majority of mortality cases. **Conclusion:** Most of the cases had multifactorial etiology. Measures for prevention, prompt recognition and specific management of neonatal seizure help to reduce the burden of neonatal morbidity in the community.

Key words: *Neonatal seizures, newborn, hypoxia-ischaemia, etiology, mortality*

A newborn with seizure represents a relatively common neonatal emergency. Even with improved perinatal care, incidence of neonatal seizures remains high. The exact incidence of neonatal seizures is unknown as many of the clinical manifestations are subtle which often escape detection and all seizure activities shown in Electroencephalography (EEG) cannot be detected clinically. Reported incidence from developed countries range from 0.1% to 0.5 % [1] and the most common etiology reported is hypoxic ischemic encephalopathy [2]. Other etiologies include septicaemia with or without CNS infection, transient metabolic disorders, intracranial haemorrhage (ICH), cerebral malformations, epileptic syndromes, inborn errors of metabolism, kernicterus and pyridoxine dependency, polycythaemia, maternal narcotic withdrawal, drug toxicity etc [2].

Early and accurate detection of seizure and its etiology is important for guiding specific therapy and to determine prognosis. Despite its clinical significance and incidence, there are number of problems in diagnosis and management [1]. 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 [3].

There is a paucity of recent data from our region and it is important to know the impact of advanced neonatal care. 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.

METHODS

This was a prospective hospital based descriptive study undertaken in a tertiary care newborn unit from September 2006 to August 2008 after getting ethical clearance from institutional ethical committee. One hundred and eight newborns, both inborn and outborn, consecutively admitted with seizures or developed seizure during the hospital stay were included in this study after getting informed consent from the parent. Seizure was defined as involuntary muscle contractions, abnormal tonic extensions or jerky movements of any part of the limb, face or mouth that was not stimulus sensitive or repetitive abnormal chewing, ocular or pedalling movements so that seizure mimics like jitteriness/tremor and benign sleep myoclonus can be excluded. Jitteriness/tremor was defined as involuntary movement of equal amplitude and faster equiphasic rhythm and benign sleep myoclonus as involuntary movement abolished by arousal, stimulus sensitive, never occur in wakefulness and with normal neurological examination [2-4]. Moribund newborns who succumb to illness and death before investigations, babies who had no documentation regarding perinatal events were excluded.

HIE was defined as neurological dysfunction with Apgar score ≤6 at 5 minutes or later or evidence of fetal or perinatal hypoxia or distress (fetal heart rate abnormalities or meconium stained amniotic fluid) or suggestive laboratory investigations (arterial pH <7 from cord blood or immediately after birth+/end organ dysfunction) [2,5,6]. Sepsis included probable sepsis (defined as clinical features with risk factors for sepsis or positive sepsis screen or radiological evidence of pneumonia) and proven sepsis (positive blood, urine or CSF culture). Evaluation included thorough search for etiology including detailed clinical history, maternal and perinatal risk factors and clinical examination. Data were collected regarding age of onset of seizure, duration and frequency of seizure and neurological examination. Maternal and perinatal history including gestational age, type of delivery, birth weight, Apgar score at 1 and 5 minutes, need for and type of resuscitation were recorded. First line investigations included routine chemistries including blood sugar, serum electrolytes like sodium, calcium and magnesium, sepsis screen, EEG and USG done in all cases. Haematocrit, creatinine kinase, liver function tests, renal function tests, lumbar puncture, neuroimaging (CT/MRI), TORCH screen, metabolic screen and ABG analysis were done wherever indicated. We followed up the babies till discharge/death. Analysis of data was done using descriptive statistics and frequencies for suitable parameters and conclusions were drawn.

RESULTS

Total 1956 neonates were admitted in NICU during study period and out of these 108 cases had seizures. In our study population, the incidence of neonatal seizures was 5.5% and male: female ratio was 1.25:1. HIE accounted for 48 (44.4%) cases of seizures either alone or in combination with other etiologies. Isolated HIE was seen in 19 (17.5%) cases and associated with sepsis in (19) 17.5% cases. Among the metabolic abnormalities associated with HIE, hypoglycaemia was the most common in 15 (13.8%) cases followed by hypocalcaemia in 2 (1.8%) cases. There was no case associated with hyponatremia and hypomagnesaemia. Sepsis accounts for 43 (37.9%) cases and associated with meningitis in 5 (4.6%), hypoglycaemia in 18 (17.3%) and hypocalcaemia in 2 (1.8%) cases. Meningitis constituted 8 (7.6%) cases and was associated with hyponatremia in 2 (1.8%) cases. Metabolic abnormalities like hypoglycaemia - 35 (32.4%), hypocalcaemia - 3 (2.7%) and hyponatremia - 1 (0.9%) account for 39 (36.1%) of total cases. Hypoglycaemia was the only primary metabolic abnormality 9 (8.3%) causing neonatal seizures in the current study. Hypoglycaemia was associated with HIE, sepsis and intracranial haemorrhage (ICH). Hyponatremia was seen in one case (0.9%) associated with sepsis and hypoglycaemia. Etiology was ICH in 8 (7.4%),

and benign neonatal convulsions in 5 (4.6%) cases. There were 2 (1.8%) cases of kernicterus, one case (0.9%) each of cerebral dysgenesis and incontinentia pigmenti.

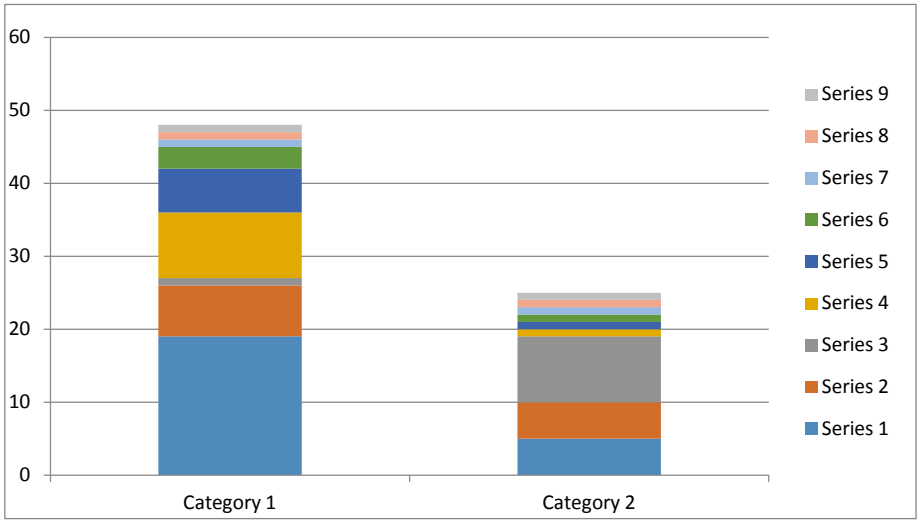

Figure 1 – Multifactorial etiology of HIE and Sepsis

Category 1 – HIE – 48 (44.4%); Series: 1) HIE – 19 (17.5%); 2) HIE + hypoglycemia -7 (6.4%); 3) HIE + hypocalcemia 1 (0.9%); 4) HIE + Sepsis – 9 (8.3%); 5) HIE + sepsis + hypoglycaemia – 6 (5.5%); 6) HIE + meningitis – 3 (2.7%); 7) HIE + sepsis + hypoglycaemia + hypocalcemia – 1 (0.9%); 8) HIE + SDH + hypoglycaemia – 1 (0.9%); 9) HIE + ICH – 1 (0.9%). **Category 2** – Sepsis 25 + 18 (included with HIE) = 43 (39.8%); Series: 1) Sepsis – 5 (4.6%); 2) Meningitis 5 (4.6%); 3) Sepsis + hypoglycaemia – 9 (8.3%); 4) Sepsis + hypoglycaemia + ICH – 1 (0.9%); 5) Sepsis + hypocalcemia – 1 (0.9%); 6) Sepsis + pyridoxine dependency – 1 (0.9%); 7) Sepsis + hypoglycaemia + hyponatremia – 1 (0.9%); 8) Sepsis + kernicterus – 1 (0.9%); 9) Sepsis + ICH – 1 (0.9%).

There was one case (0.9%) of pyridoxine dependency, confirmed by therapeutic response to pyridoxine administration. Etiology is unknown in 13 (12%) cases. EEG was done in 80 cases and was abnormal in 75% of cases. Abnormal wave pattern with spikes in 19 (31.6%) cases, abnormal pattern with slow waves and focal sharp waves in 13 (21.6%) cases, abnormal pattern with generalised voltage suppression in 15 (25%) cases, multifocal origin in 11 (18.3%) cases, abnormal focal seizure pattern from right temporo-parietal region in 2 (3.3%) cases. Out of 36 HIE babies, who underwent EEG, 14 HIE II babies and 22 HIE III babies had abnormal EEG. Suppressed background activity was present in 10 cases of HIE III babies.

Mortality in this study was 16 (17.2%) out of which 10 (62.5%) were males and 6 (37.5%) were females. The most common cause was a combination of HIE and sepsis. A single etiology was present only in 3 cases. Two had HIE and other baby had sepsis.

DISCUSSION

Incidence of neonatal seizures in current study was high compared to latest reported literature from developed countries [1]. A true incidence of neonatal seizure based on total live births cannot be calculated as most of the cases were referred from peripheral hospitals. Reasons for high incidence may be the higher rates of prematurity, small for gestational age babies, maternal diseases like gestational diabetes mellitus, pregnancy induced hypertension and related perinatal obstetric complications. Incidence can be reduced by good

antenatal and perinatal care. Non-availability of video EEG and aEEG (amplitude integrated EEG) might have resulted in inclusion of seizure mimics in our study population [7]. The current study shows a male preponderance which is noted by early researchers also [8].

The most common etiologies of neonatal seizures in our study include HIE and sepsis which are still common in both developed and developing countries [3,9-13]. They are preventable to some extent with regular antenatal check-ups, advanced perinatal care giving stress for hospital delivery and the importance of conducting delivery and resuscitation by trained hands and prevention and proper treatment of infections. Neonatal sepsis constituted an important etiology of neonatal seizures which is the second most common etiology in the current study [14]. It emphasises the need for screening high risk and sick new-borns for these etiologies. Incidence of meningitis is low in comparison to other studies which might be due to early administration of antibiotics in sick suspected sepsis cases prior to lumbar puncture. Infections can be prevented by regular sterilisation, aseptic precautions, safe injection practices and appropriate antibiotic administration in NICU.

Incidence of hypoglycaemia is high compared to other studies probably due to high incidence of gestational diabetes and prematurity in our community [11-12]. Although, hypocalcaemia has been reported as the most common metabolic abnormality in literature [10], incidence of hypocalcemia was low in our study which can be due to timely administration of calcium in at risk neonates. Proper monitoring and fluid electrolyte management is essential to tackle metabolic abnormalities. Intracranial haemorrhage (ICH) is an important cause of neonatal seizure which is high in our study as compared to other studies [8]. Conducting delivery by experienced person can reduce birth injury. Increased detection due to sophisticated radiological evaluation may be other cause.

Number of cases of kernicterus in our study was low as compared to that in other studies probably due to early detection, referral and prompt management of jaundiced newborn [15]. Incidence of cerebral malformation is low [11,16] which may be due to non-feasibility of advanced radiological evaluation like MRI in all cases which also may be the reason for high incidence of unknown etiology in our study [11,17,18]. MRI is a helpful tool in detecting periventricular white matter lesions but has inherent difficulty in patient preparation, safety and timing. Case of Incontinentia pigmenti presented with history of consanguinity, typical skin lesions and seizure in day 4 of life [19]. We were unable to do investigations like MRI, TORCH screen and IEM screen in some of the cases due to financial constraints which also have resulted in more number of idiopathic cases.

The mortality in the present study is comparable to that described in literature but remain high as compared to reported mortality in developed countries [20]. The most common cause of mortality is a combination of HIE and sepsis. Abnormal EEG with supressed background activity is present in majority of them [10]. Abnormal inter-ictal EEG mainly concerning background activity pattern is described as a major predictor of disease severity and outcome [20-21]. Etiology and EEG were the important predictors of outcome [20].

There are some limitations of our study e.g. clinically evident seizures only were included in the current study; hence, very subtle and electrical only seizures might have been missed. Non-availability of synchronised video EEG and aEEG might have resulted in inclusion of newborns with seizure mimics. Video EEG and aEEG help in prompt recognition of seizures and should be made available in NICU as electro clinical dissociation is common in newborns. A true incidence of neonatal seizure based on total live births could not be calculated as most of the cases were referred from peripheral hospitals. We could not get many advanced investigations in our study; therefore, HIE and sepsis remains the most common causes even though the number of recognised etiologies of neonatal seizures had increased due to advances in neonatology and investigations.

CONCLUSION

Incidence of neonatal seizure was 5.5%. Multifactorial etiology in majority of cases of neonatal seizure is the highlight of this study which emphasise the need for extensive evaluation of all cases of neonatal seizure for possible etiologies. It helps in proper management and prevention of further injury thus reducing the burden of neonatal seizure in the community.

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Funding: None *Conflict of Interest: None Stated*

How to cite this article: Anand V, Pillai SK, Jayakrishnan D, Nair PMC. Neonatal Seizures: our experience of incidence, etiology and outcome in a tertiary care centre. Indian J Child Health. 2014;1(2):39-43.

Doi: 10.32677/IJCH.2014.v01.i02.001