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Original Research Article

Clinical profile, etiology, type and outcome of neonatal seizures: a hospital-based study

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ABSTRACT

Background: Our study was undertaken to study the etiological factor, clinical profile, types and outcome of newborn with neonatal seizures (NNS).
Methods: Our study was hospital based prospective study was done in Sheri Kashmir institute of medical sciences (SKIMS) Bemina from April 2013 to April 2015 in NICU, after obtaining ethical clearance from institutional ethical committee. All neonates fulfilling inclusion criteria were included in our study.
Results: In our study, 80 neonates with seizures were included in our study, among them 48 were males and 32 were females. Majority of neonates (57.5%) developed seizures during first 72 hours of life due to birth asphyxia. Commonest types of neonatal seizures observed in our study were subtle observed in 46 cases, followed by tonic (21.2 %), clonic (14.9 %) and mixed (6.2%) seizures. Birth asphyxia was commonest cause (57.5%) of NNS, sepsis with meningitis (18.7%) followed by hypoglycemia (13.7%) and hypocalcemia (5%). Cases of birth asphyxia were associated with higher mortality (58.3%) as compared to cases with metabolic seizures.
Conclusions: From our study we conclude that commonest cause of neonatal seizure was birth asphyxia occurring within 72 hours of birth. Sepsis and meningitis were also common infections resulting in neonatal seizure, while as hypoglycaemia and hypocalcemia were common biochemical abnormalities leading to NNS. Early identification and treatment are likely important for long-term outcomes in acute symptomatic seizure.

Keywords: NNS, Neonate, Etiology and subtle seizures

INTRODUCTION

Neonates are at greater risk for the development of seizures, because various metabolic, structural, toxic and infectious diseases occur more during neonatal period compared to other age groups.[1] NNS are categorised as acute symptomatic or provoked seizures, acute symptomatic seizures are defined as seizures resulting from an acute brain injury like trauma or brain infection, stroke, while as provoked seizures are defined as seizures occurring from reversible and transient brain alterations toxic or metabolic origin.[2] Besides this, unprovoked seizures occur less frequently in the neonatal period, and are defined as seizures occurring beyond the interval period estimated for acute symptomatic seizures occurrence or occurring without causative clinical condition.[3,4] Unprovoked seizures may result secondary to prenatal ischemic lesions or structural abnormalities of brain like cortical malformations.[5]

NNS are relatively common, occurring in 1.8 to 3.5 per 1000 live births, with increased frequency in premature or low birth weight babies in comparison to term babies.[6] Also, neonates have immature neurons and differences in levels of neurotransmitter make them susceptible to seizures, as immature neurons contain a larger number of

excitatory receptors i.e., N-methyl-D-aspartate (NMDA) and α-amino-3-hydroxy-5-methyl-4-isoxazolpropionic acid (AMPA) re and fewer inhibitory receptors gamma-aminobutyric acid (GABA), therefore being one of reason of low seizure threshold in neonates.[7] NNS are commonly as result of underlying cerebral or biochemical abnormalities, while as in 10% of cases no cause has been ascertained.[8] Moreover, incidence is as high as 10-25% in NICU, among which about 35 to 40% will have major neurological sequelae and mortality is 15%.[9]

The most widely used clinical classification of NNS is by Volpe into 5 main types which shows seizure type, incidence with clinical signs as follows-1. Subtle seizures commonest: 50% and lip smacking, sucking or chewing and tongue protrusion pedalling, swimming, horizontal or persistent deviation of eyes, gaze fixation sudden arousal with episodic limb hyperactivity and crying. 2. Tonic: 5% and sustained increase in muscle tone extension or flexion of limbs for few seconds to minutes, 3. Clonic: 25% and rhythmic muscle jerking in one (focal) or more body parts (multifocal), 4. Myoclonic: 20% and rapid, single or arrhythmic repetitive jerks, 5. Non-paroxysmal repetitive behaviours.[10]

Commonest cause of NNS is birth asphyxia, while other causes include septicaemia with or without CNS infection, intracranial bleed and transient metabolic disorder.[11,12] Outcome is predicted by the underlying aetiology.[13] Patients with hypoxic ischemic encephalopathy (HIE), intra-ventricular haemorrhage and structural brain malformation have the worst prognosis while as those with transient metabolic abnormalities and benign familial or idiopathic aetiologies have better prognosis.[13.14] Aetiology of NNS is identified in 99% of cases and is rarely idiopathic.[12] Synchronised video-EEG monitoring is non-existent practically in NICU in developed countries, therefore clinical observation remains key to diagnosis in NNS.[15]

The present study was planned to evaluate the different causes, clinical characteristics, types and outcome of NNS, so that effective strategy can be formulated for management of NNS.

METHODS

This was a prospective hospital based descriptive study undertaken at Sheri Kashmir institute of medical sciences (SKIMS) Bemina from April 2013 to April 2015 in NICU, after obtaining ethical clearance from institutional ethical committee. Eighty neonates 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 parent.

Inclusion criteria

Neonates (up to 28 days of life) presenting with at least one of the following clinical type of seizures: Generalized tonic seizures, focal or multifocal clonic seizures, subtle activity with apnea or autonomic features and myoclonic seizures were included in the study.

Exclusion criteria

Babies >28 days of life, seizure like activity (jitteriness, tetanic spasm) and Subtle activity without autonomic features or apnea were excluded from the study.

Detailed antenatal, natal and post-natal history along with clinical examination and laboratory evaluation were obtained in all studied neonates. Perinatal history like 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. Apgar score was noted and done, birth asphyxia was diagnosed if baby did not cry for more than three minutes after birth or documented Apgar score was ≤3 at one minute and <7 at 5 minutes of birth. Also, post-natal history like lethargy, poor feeding, jaundice, excessive cry, fever, vomiting and seizures were taken. Detailed examination like vitals of baby (Heart rate, respiratory rate, peripheral pulses, blood pressure, temperature, and capillary filling time) were recorded. General physical examination of neonate was done according to the proforma and any disparity in head size and shape, gestational age was assessed according to New Ballard scoring. CNS examination was done as per the proforma along with systemic examination. The following investigations were done for NNS: complete blood count (haemoglobin, total count, differential count), KFT, sepsis screening: CRP and blood culture, blood glucose (Hypoglycemia if RBS is less than 40 mg / dL), serum electrolytes (hypo or hypernatremia i.e., serum sodium <130 or >150 meq/l, serum calcium (hypocalcemia serum calcium <8 mg/dl), sodium and potassium were done. Cerebrospinal fluid (CSF) was done in suspected meningitis or septicaemia while as cranial ultrasound was done to find out any intraventricular haemorrhage, hydrocephalus and any malformation.

Analysis of data was done using Microsoft excel and online calculators, while descriptive statistics and frequencies were used for suitable parameters. Chi square test was used for statistical analysis, while as $p<0.05$ was considered significant.

RESULTS

In our study, 80 neonates with seizures were included in our study, among them 48 (60%) were males and 32 (40%) were females. In present study, out of 80 babies, 71 were full term. Among these 59 full term neonates (58.82%) were appropriate for gestational age (AGA) and 12 (21.6% were small for gestational age (SGA), there were 8 (18.6%) preterm babies and 1 post term baby).

Table 1: Distribution of NNS according to gestational age and gender distribution in NNS.

Variables	Frequency	Percentage (%)	P value
Gestational age			
AGA	59	73.7	<0.001
SGA	12	15	
Preterm	8	10	
Post term	1	1.2	
Gender			
Males	48	60	0.074
Females	32	40	

Out of 80 cases, 9 were born at home and 71 (87.25%) at hospital. Out of hospital deliveries 60 were inborn and 11 were out born. Among 80 neonates 43 were born by vaginal delivery, 31 were delivered by LSCS and 6 were born by assisted delivery.

Table 2: Place and type of deliveries of babies with NNS.

Variables	Frequency	Percentage (%)	P value
Place of delivery			
Home delivery	9	11.2	<0.001
Hospital (inborn)	60	75	
Hospital (outborn)	11	13.7	
Type of delivery			
Normal vaginal	43	53.7	<0.001
LSCS	31	38.7	
Assisted vaginal	6	7.5	

In study, onset of seizures on 1st day of life was seen in 29 neonates (36.27%), on 2nd day of life 18 neonates developed seizures (27.45%), on 3rd day of life 11 (16.67%) babies developed convulsions. First 3 days of life together constituted >70% of NNS. From 4th to 7th day 15 babies developed seizures, while as 7 babies developed seizures after 1 week.

Besides this, 46 patients had subtle seizures, 17 had generalised tonic seizures, 7 multifocal clonic seizures and 5 (5.9%) had focal clonic seizures. Five neonates had mixed type of seizures, among these 3 had subtle with generalized tonic and 2 had subtle with clonic seizures.

Table 3: Time (days) of onset of NNS.

Day of onset of NNS	Frequency	Percentage (%)	P value
1	29	36.2	<0.002
2	18	22.5	
3	11	13.7	
4 to day 7	15	18.7	
>7 to 28	7	8.75	
Total	80	100	

Table 4: Type of NNS.

Type of NNS	Frequency	Percentage (%)	P value
Generalised tonic	17	21.2	<0.001
focal clonic	5	6.2	
Multifocal clonic	7	8.7	
Subtle	46	57.5	
Mixed			
Subtle with generalised tonic	3	3.7	
Subtle with clonic	2	2.5	
Total	80	100	

Birth asphyxia is the commonest cause of NNS in our study. The 46 babies had birth asphyxia (55.9%), 11 babies had hypoglycemia (17.6%), 15 babies had sepsis with meningitis (12.7%), 4 babies had hypocalcemia (2.9%), 1 baby had intraventricular hemorrhage (2.9%) and in 3 cases no cause was ascertained.

Table 5: Etiology of NNS.

Etiology	Frequency	%	P value
Birth asphyxia	46	57.5	<0.001
Hypocalcemia	4	5	
Hypoglycemia	11	13.7	
Sepsis with meningitis	15	18.7	
Intraventricular haemorrhage	1	1.25	
Others	3	3.7	

Table 6: Correlation of etiology with day of onset of NNS.

Day of onset of NNS	Etiology, n (%)					Total (%)	P value
	Birth asphyxia	Metabolic		Sepsis			
		Hypoglycemia	Hypocalcemia	Sepsis with meningitis	Others		
1	36 (100)	-	-	-	-	36 (100)	<0.001
2	7 (43.7)	5 (31.2)	2 (12.5)	1 (6.2)	1 (6.2)	16 (100)	
3	2 (25)	3 (37.5)	1 (12.5)	2 (25)	-	8 (100)	
4-7	1 (11.1)	2 (22.2)	-	5 (55.5)	1 (11.1)	9 (100)	
8-28	-	1 (9.1)	1 (9.1)	7 (63.7%)	2 (18.1)	11 (100)	
Total	46	11	4	15	4	80	

P<0.001 (statistically significant for onset of seizures in first week of life with birth asphyxia).

Table 7: Correlation of etiology of NNS to gestational age.

Etiology	Gestational age, n (%)				Total (%)	P value
	Term aga	SGA	Preterm	Post term		
Birth asphyxia	37 (80.4)	6 (13)	2 (4.3)	1 (2.1)	46 (100)	<0.001
Sepsis with neonatal meningitis	11 (73.3)	2 (13.3)	2 (13.3)	-	15 (100)	
Hypoglycemia	6 (54.5)	4 (36.3)	1 (9.1)	-	11 (100)	
Hypocalcemia	3 (75)		1 (25)	-	4 (100)	
IVH	-	-	1 (100)	-	1 (100)	
Others	2 (66.6)	-	1 (33.3)	-	3 (100)	
Total	59	12	8	1	80 (100)	

In the present study, out of 59 term AGA babies, 37 had birth asphyxia. Out of 8 preterm babies, 1 had hypoglycemia, 2 had asphyxia and 1 had hypocalcaemia and 2 had meningitis and 1 had IVH. Out of 1 post-term baby 1 had birth asphyxia. Low birth weight babies (<2.5 kg) are more prone for seizures due to hypoglycemia with statistically significant p<0.001.

DISCUSSION

In our study, among 80 neonates with seizures 71 were full-term neonates (88.7%), of which 59 (73.7%) were AGA i.e., B. Wt. ≥2500 gm and 12 (15%) were SGA i.e., <2500 gm, 8 were preterm babies (10%) and 1 was post term baby. In our study NNS were common in term neonates which is consistent as reported by other studies.[12]

Incidence of NNS in current study was high compared to studies from developed countries.[16] 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.[17] Our study shows male preponderance (40%) which is consistent as reported by other studies.[18]

As reported by Mahaveer et al majority of cases with NNS (68.7%) were born by normal vaginal delivery followed by (28.1%) by LSCS and 3.1% by forceps delivery, which is consistent as seen in our study.[19] Among 80 neonates 43 (53.7%) were born by vaginal delivery, 31 (38.7%) were delivered by LSCS and 6 (7.5%) were born by assisted delivery.

In our study, most common etiologies of NNS include birth asphyxia (57.5%) and sepsis (18.7%) which are consistent and still common in both developed and developing countries as reported by other studies, therefore aseptic precautions, proper sterilisation with appropriate antibiotic administration should be implemented to prevent infections in NICU.[15,20]

In our study, majority of neonates (36 neonates) convulsed on first day of life,while as majority of newborns with hypoglycaemia (31.2%) had seizures on second day of life and in majority of babies with meningitis (63.7%) convulsed after one week which is consistent as reported by other studies.[21]

In our study, main metabolic abnormalities like hypoglycemia and hypocalcemia were found in 13.7% and 5% cases of NNS as reported in other studies.[22,23]

In our study, commonest type of NNS were subtle seizures 46 (57.5%) patients had subtle seizures, 17 (21.2%) had generalised tonic seizures, 7 (8.7%) had multifocal clonic seizures and 5 (6.2%) had focal clonic seizures while as 5 neonates had mixed type of seizures, among these 3 (3.7%) had subtle with generalized tonic seizures and 2 (2.5%) had subtle with clonic seizures, similar results are also reported by other studies.[19,24]

In our study, 68 (85%) patients of NNS were discharged successfully, among them 12 cases of NNS expired. Best prognosis is seen in cases of NNS caused by transient metabolic abnormalities and subarachnoid bleed, while as worst prognosis is reported in cases with neonatal seizures caused by birth asphyxia and brain abnormalities.[25] Patients with meningitis have intermediate prognosis, which is concordant as reported in our study where mortality was seen in 12 (15%) cases of neonatal seizures, and commonest cause seen was birth asphyxia in 7 cases (58.3%) followed by sepsis and hypoglycaemia.[22]

Limitations

The main limitation in our study was small sample size, in addition in our study only clinically evident seizures only were included, as a result of these electrical only seizures and very subtle seizures might be missed. Also, non- availability of synchronised aEEG and video EEG results in inclusion of neonates with seizure mimics**.**

CONCLUSION

From our study we conclude that in majority of cases of neonatal seizures cause was apparent, birth asphyxia was the main cause identified in cases of neonatal seizures. However, identification of etiology is helpful regarding treatment and prognosis in neonatal seizures. Besides

these transient metabolic abnormalities like hypoglycaemia (particularly common in low-birth-weight babies) and hypocalcemia also result in neonatal seizures, timely intervention can prevent further brain damage in these conditions. Also, time of onset is associated with etiology in neonatal seizures, with birth asphyxia commonly occurring in first three days of life, while CNS infections occurring after one week. Subtle seizures were most common neonatal seizures in our study.

Neonatal seizure is mostly associated with perinatal complications, therefore continued advances in neonatalogy may reduce incidence of seizures and further prevent cognitive, neurological, epileptic and cognitive consequences of NNS in neonates.

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