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Clinical profile and etiology of neonatal seizures in NICU Rims, Raichur

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Abstract--Introduction: Seizures are more common in the neonatal period than in any other stage and affects approximately 1% of all neonates. Amongst neurological disorders, seizures are the most common in neonates. The study was conducted to determine the aetiology and clinical profile of neonatal seizures. Materials and Methodology: This study was designed to be a hospital based prospective observational study was undertaken in the in the hospital attached neonatal intensive care unit (NICU), RIMS, Raichur. A total of 500 neonates presenting with seizures or who developed seizures in hospital from 01 February 2022 to 31 May 2022 were enrolled in the study. All neonates (age 0 – 28 days) who presented to the hospital with history of seizures or who develop seizures during the course of hospital stay were taken into study. Detailed antenatal history examination and clinical details of each seizure episode reported by the mother and subsequently observed by the resident doctors on duty were recorded. Results: Among these 405 patients (81%) were from rural areas and 95 patients (19%) were from urban areas. Males comprised 280 patients and females comprised 220 patients Gestational age Out of 500 neonates admitted with seizures, 365 (73.1%) were term and 135 (26.9%) were preterm. Extremes of maternal age viz. ≤ 18 years or ≥ 40 years comprised 7%, while 93% comprised in the age group of 19-39 years. 53% (n=265) neonates were born to nulliparous women, while parous women comprised 47% (n=235). 39.4% (n=197) of cases were born by caesarean section while 60.4% (n=302) were born by vaginal delivery. Conclusion: The most frequent episodes of seizures were observed in the first 72 hours of

life. In HIE most of the patients developed within first 24 hours of life. In case of meningitis, seizures were reported to be more common after 72 hours of life. Subtle seizures were reportedly the commonest type that was observed among the study participants, followed by focal clonic seizures.

Keywords---neonatal seizures, aetiologies, clinical profile, neurological problem.

Introduction

Almost around 1% of all the neonates were most frequently affected with seizures than individuals with any other age group/category.¹ Amongst all the neurological disorders, seizures are reported to be the most common in the neonatal period.² The term 'seizure' could be defined as the clinical paroxysmal alteration in neurologic function, i.e., motor, behavioural and/or autonomic function. The fundamental mechanisms of all the reported neonatal seizures are mostly unknown, disturbance in energy production could possibly result in the failure of Na⁺/K⁺ pump. Additionally, these cellular observable factors, differential development of neural systems might enhance the excitatory state of the immature brain and eventually predispose to the development of seizures. Other suggested mechanisms of this injury could be attributed to the effects of nitric oxide synthase inhibition on cerebral circulation which in turn leads to ischemic cerebral injury.³

The International League Against Epilepsy classification adopted by WHO, still includes neonatal seizures under an unclassified category.⁴ Historically, seizures were basically divided in following clinical categories viz focal clonic, multifocal clonic, tonic, myoclonic and subtle seizures.⁵ Diverse medical conditions present in the newborn could be associated with neonatal seizures. Hypoxic-ischemia is almost traditionally considered as the most common aetiology of the neonatal seizures.^{5,6} Cerebral infarction and stroke are the common underlying conditions which had reported to be the second most common cause of neonatal seizures occurring in otherwise well term infants, without any history of previous risk factors.⁷ Hypoglycaemia is also one of the well-known causes of neonatal seizures.

Infants presented with sepsis and meningitis clinically presented to have hypoglycaemia which can be attributed to the fact due to inadequate intake, increased metabolic rate and reduced ability to metabolize glucose as well.⁸ Hypocalcaemia is the one condition where total serum Ca levels falls below 7mg/dL where the optimum level below which seizure happens is still debatable. Late onset hypocalcaemia could be due to the use of high phosphate infant formula which has been cited as common aetiology of the neonatal seizures.^{9,10} Therefore, the most commonly presented hypocalcaemia present in infants with trauma, haemolytic disease, asphyxia usually coexist with hypoglycaemia and hypomagnesemia and most frequently presents at 2-3 days of life. Hypomagnesemia is the condition where the serum magnesium level falls below 1.5mg/dL can rarely manifest with tetany and the development of seizures at 2 -

4 weeks of age and most commonly associated with secondary hypocalcaemia. Magnesium depletion is well-known to predispose to decreased PTH secretion.

Hyperphosphatemia might be caused by the ingestion of milk formulas containing high amounts of phosphorous, excessive parenteral administration of phosphorus could lead to impaired renal function and hypoparathyroidism. Hyponatremia can occur which is considered as a result of fluid overload, renal compromise and SIADH (syndrome of inappropriate ADH secretion) can be a frequent complication of neonates with birth asphyxia. Clinical outcome is usually predicted by the underlying aetiology that is detected in the neonates.¹¹ Patients with hypoxic ischemic encephalopathy (HIE), intra-ventricular haemorrhage and structural brain malformation usually reported to have the worst prognosis.^{11,12} while those reported with transient metabolic abnormalities and benign idiopathic or familial aetiologies have the best prognosis comparatively. Hence, the present study was conducted with the aim and objective involving the Assessment of Clinical Profile and Etiology of Neonatal Seizures in the Neonatal intensive care unit, RIMS, Raichur.

Materials and Methodology

This study was designed to be a hospital based prospective observational study was undertaken in the in the hospital attached neonatal intensive care unit (NICU), RIMS, Raichur. A total of 500 neonates presenting with seizures or who developed seizures in hospital from 01 February 2022 to 31 May 2022 were enrolled in the study. All neonates (age 0 – 28 days) who presented to the hospital with history of seizures or who develop seizures during the course of hospital stay were taken into study. Detailed antenatal history examination and clinical details of each seizure episode reported by the mother and subsequently observed by the resident doctors on duty were recorded. Blood sugar was done and venous blood was collected as soon as possible and blood glucose, total serum calcium levels, Na⁺, K⁺, Mg and Phosphorus levels were done immediately after baby had seizures and before instituting any treatment. In addition, complete blood counts, blood culture, USG cranium, MRI/CT, CSF analysis, serum lactate and ammonia, TMS, urinary GCMS and TORCH antibody titres were done as per the requirement in individual cases. Data was entered in a Microsoft excel spreadsheet. Continuous variables were summarized as mean and standard deviation. Categorical variables were summarized as percentage.

Results

Out of all the patients admitted in NICU, RIMS from 1st February 2022 to 31st May 2022, 500 neonates were diagnosed as having neonatal seizures. A hospital-based seizure prevalence of 2.03% was thus observed. However, in Preterm babies this prevalence was much higher at 11.76% (table-1). Among these 405 patients (81%) were from rural areas and 95 patients (19%) were from urban areas. Males comprised 280 patients and females comprised 220 patients Gestational age Out of 500 neonates admitted with seizures, 365 (73.1%) were term and 135 (26.9%) were preterm. Extremes of maternal age viz. ≤ 18 years or ≥ 40 years comprised 7%, while 93% comprised in the age group of 19-39 years. 53% (n=265) neonates were born to nulliparous women, while parous women comprised 47% (n=235).

39.4% (n=197) of cases were born by caesarean section while 60.4% (n=302) were born by vaginal delivery.

Majority of neonatal seizures occurred within the first few days of life, with first 03 days accounting for 76% of neonatal seizures. In HIE seizures occurred in the first few days of life with majority occurring in the first 24 hours of life. In our study 61% of seizures due to HIE occurred within first 24 hours of life and 92% of seizures occurred within 48 hours of birth. In meningitis seizures were more common after first 3 days of life. 92% of seizures occurred after 3rd day of life, among these 30% cases presented after 1st week of life. Hypocalcemic seizures had a dual distribution regarding the age of onset. In preterm neonates Hypocalcemic seizures were more common in the first 72 hours of life. In neonates who had hypocalcemia, likely due to high phosphate formula feeds, seizures occurred after first week of life (table-4,5).

Table 1
Presenting characteristics of the cases

Variables		N	%
Gender	Male	280	55
	Female	220	45
Gestational age	Very preterm	7	1.6
	Moderate preterm	39	7.5
	Late preterm	116	23.3
	Term	338	67.5
	Post term	0	0
Birth weight	Normal	313	62.5
	Low birth weight	187	37.5

Table 2
Maternal Characteristics of the Neonates

Characteristics	Variables	N	%
Maternal age	≤ 18	4	0.83
	19 – 29	250	50
	30 – 39	213	42.5
	≥ 40	33	6.6
Maternal parity	Nulliparous	238	47.5
	Parous	262	52.5
Delivery type	Caesarean section	204	40.8
	Vaginal	296	59.1
Labour record foetal distress		113	22.5

Table 3
Aetiology of neonatal seizures

Aetiology	N	%
HIE	292	58.3
ICH	33	6.6
Meningitis	59	11.6

TORCH infections	4	0.83
Hypocalcaemia	38	7.5
Hypoglycaemia	29	5.8
Hypomagnesemia	4	0.83
IEM	4	0.83
Epilepsy syndromes	4	0.83
Unknown	33	6.6

Table 4
Distribution of various aetiologies among Term and Preterm neonates

Gestation		HIE	ICH	Meningitis	Hypercalcaemia	Hypoglycaemia
Term	N	230	21	46	17	19
	%	67.9	6.1	13.5	4.9	3.7
Preterm	N	54	29	21	16	12
	%	33.3	17.9	12.8	10.2	7.6

Table 5
Distribution of primary metabolic seizures among Term and Preterm neonates

Metabolic abnormality	Term	Preterm
Hypocalcaemia	17	16
Hypoglycaemia	19	12
Hypomagnesemia	0	1

Discussion

The most frequent signs of any neurological dysfunction reported in a neonate is detected to be seizures. Since the development of seizure may be the only sign of any CNS disorder, their diagnosis plays a very important role in the field of clinical medicine. Since they are considered as the powerful predictors of long term cognitive and developmental impairment in a neonate. Seizures are not only the most frequently observed during the neonatal period, they also pose more difficulty in diagnosing the underlying condition because of the subtle behavioural nature and EEG manifestations. This study comprised of about 500 cases of neonatal seizures who were admitted in Neonatal intensive care unit (NICU), RIMS, Raichur over the period of one year were included up for the study. 45% were female (220 cases) and 55% were male (280 cases) reporting no definite sexual predominance which are in correlation with earlier study of *Sheth* RD at al¹⁴ reported with 37% of the babies were preterm (34 cases) 48% had low birth weight.

The most commonly identified risk factors that were associated with neonatal seizures are prematurity and low birth weights and the underlying conditions such as birth asphyxia sepsis and intra cranial bleeds are reported to be the common etiological factors for neonatal seizures. The average age at onset of seizure in term new born during first week of life was 2.83 days. While that in pre term was 2.5 days. 33% of term and 32% of pre-term had seizures on the first day of life. 86.5% term and 94% of pre term has seizures with in the first week. 59.1%

of babies were delivered vaginally. 32.6% accounted for home delivery and 26.5% were delivered by outlet forceps. High incidence of home deliveries is the probable aetiology for birth asphyxia. Family History of seizures was observed in 4 cases.

The other abnormalities that were found associated with oedema and haemorrhage (Hydrocephalus was observed in 7 cases mostly in sepsis and meningitis. 6 cases of decreased ventricular size have been seen mostly in HIE. The incidence of haemorrhage is lower when compared to earlier study of *merchant et al*¹⁵ in 1987. The prognosis of haemorrhage is at times identical to that obtained in the earlier studies. EEG has been done in 63 cases. abnormalities were observed in 17 cases (26.2%). 74% had no EEG abnormalities. this is slightly higher than 19% of 243 analyzed seizures shown in a retrospective evaluation by *weiener et al*.¹⁶ Most of the subtle seizures did not have an EEG correlation to be found out. This is in similarity with the results obtained in the earlier study by *Mizrahi and Kellaway*¹⁷ in 1980.

Hypoglycaemia was observed in 29 cases out of which 8 were due to isolated hypoglycaemia which had normal clinical outcome. 11 were associated with HIE, while 10 cases were along with sepsis and meningitis. Hypocalcaemia was observed in 38 cases of which 16 were along with HIE and 8 with sepsis and meningitis. There were 14 cases of meningitis as detected by CSF analysis. Lumbar puncture was done in all cases of suspected sepsis and meningitis. The most common type of seizures in this study in both term and preterm babies were subtle seizures. Least common type in term babies was reported to be myoclonic seizures, whereas in preterm babies least common type of seizures was myoclonic and multifocal clonic seizures. The results were in correlation with the values inferred from the previous study of *Moayedi AR, Zakeri S et al*.¹⁷ Term babies had a better outcome than preterm babies. Mortality rate was reportedly higher in preterm babies. In both term and preterm babies unifocal clonic seizures had best prognosis. The most common causes of seizures in this study were HIE and neonatal sepsis. Out of all the cases of sepsis 25% were culture positive. In 30.5% of sepsis cases seizures were due to metabolic abnormalities like hypoglycaemia and hypocalcaemia and one case of Kernicterus. In most of the cases there was a combination of etiological factors.

Phenobarbitone was effective in controlling seizures in 50% of the patients with a single loading dose. When combined together, phenobarbitone and phenytoin were effective in 75% of the reported cases. This is slightly higher than the results obtained (60%) when both the drugs used together in earlier studies by *Painter et al*¹⁸, in 1999. Midazolam proved effective in 2 cases and seizures responded to pyridoxine in one case. The mortality in neonatal seizures in this study was 23%. Hypoglycaemia not associated with HIE, Sepsis and meningitis and HIE stage III had very poor outcome in both term and preterm babies. The other causes of mortality were kernicterus, Encephalocele. Deaths were associated with severe cerebral oedema, multiple ischemic hypo densities, intra cerebral haemorrhage, and abnormal EEG records and poor response to anti-epileptic drug therapy.¹⁹

Conclusion

The most frequent episodes of seizures were observed in the first 72 hours of life. In HIE most of the patients developed within first 24 hours of life. In case of meningitis, seizures were reported to be more common after 72 hours of life. Subtle seizures were reportedly the commonest type that was observed among the study participants, followed by focal clonic seizures. Generalized tonic seizures were the most common type of seizures in neonates with CH. Around 55% neonates had a biochemical anomaly either alone or in relation with other aetiologies. Secondary metabolic abnormalities were also reported to be more common in HIE where in hypocalcaemia was the commonest type in primary metabolic seizures followed by hypoglycaemia.

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