www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i3.185

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Comparison of Clinical and Etiologic Profile of Neonatal Seizures Over A Decade.- A Hospital Based Prospective Study

Authors
Geetha S[1], Sanuja Sarasam E[2], Mary Iype*[3], Sobha Kumar S[4]
[1,2]Asst Professor, [3]Addl. Professor, [4]Professor
Department of Pediatrics & Pediatric Neurology, Government Medical College, Thiruvananthapuram, India
Corresponding Author
Geetha .S
Email: *geethapmohan@yahoo.com*

Abstract
Seizure is occurrence of signs and symptoms due to excess neuronal activity of brain. It signifies neurologic dysfunction in neonatal period. Hence neonatal seizures are a medical emergency. The most important factor that predicts their outcome is the underlying etiology. Kerala is in forefront of health indicators in children and neonates. Our neonatal unit has provided neonatal care in our state over many decades. The present study was a comparative study to look into the prevalence of neonatal seizures& compare etiology in a decade apart.
Objective: *To compare the clinical and etiologic profile of neonatal seizures in neonates over decade.*
Design: *Prospective hospital based study done in 2004 and 2014. Setting: The neonatal intensive care unit (NICU) of a tertiary care hospital. Participants: In 2004, over 6 months,135 babies were recruited . In 2014,156 neonates were recruited over one year.*
Methods: *The neonates with seizures in neonatal period were assessed clinically and the etiology is studied. The clinical and etiologic profile were compared.*
Result: *The proportion of admissions as neonatal seiures in 2014 was 4.77%. Pregnancy induced hypertension was the commonest maternal risk factor (48%) followed by gestational diabetes (40.5%). The common causes for seizures remained same in both period. HIE followed by hypoglycemia, hypocalcemia and intracranial bleed also contributed. Newer investigative modalities like ultrasound scan was done in 59.5% in 2014.In 2004, the study was done for prognostic outcome, hence, EEG was done in 128 cases and CT scan was taken at follow up in 130 cases.*
Conclusions: *The proportion of neonates admitted with seizures were more in 2004 when compared with 2014.The use of non invasive USS head was more in 2014. The common etiology of neonatal seizures remained same across decade.Most common cause was HIE followed by hypoglycemia.*
Keywords: *Neonate, Seizures, comparison, clinical, etiology.*

Introduction

Neonatal seizures is a medical emergency. Prompt and timely diagnosis and management improves survival and reduces sequalae.[1] There are challenges in evaluation and intervention in neonates as the clinical manifestations of seizures in this age group is different from old children. Brain injury from antenatal period can extend into this period. A seizure is defined clinically as a paroxysmal alteration in neurologic function, i.e.

motor, behavior and/or autonomic function.[2]Many systemic illness also results in seizures like hypoglycemia, hypocalcaemia etc.[3,4] Prompt recognition of cause is important management.

Kerala is in forefront of many health indicators in our country. Our IMR is low when compared to other Indian states. NFHS 4 has quoted IMR of Kerala to be 6/1000.[5] This even less than SDG for envisaged for Kerala[8].Our hospital is the forerunner in health care of neonates and children over decades.

Hypoxic ischemic encephalopathy (HIE), intracranial infections, metabolic disorders such as hypoglycemia, hypocalcaemia, hyponatremia, intracranial hemorrhages (ICH), inborn errors of metabolism (IEM) and epileptic syndromes are the common causes of neonatal seizures.[6]

Ultrsound scans are non invasive technology available for assessing neonatal seizures. But due to difficulty, the need for a neuro imaging is assessed on a case by case basis. In 2004, ultrasound scans were available sparingly, but in 2015 they are done in high rates. We have done this study to compare the proportion of neonates with seizures in our neonatal Intensive care unit and also to compare the clinical & etiologic profile across a decade. A similar study was done by Iypeetal in 2004.[6]They have studied the prognostic factors in a followup study. The etiology was reported in a separate study.[7]

Period of study: November 2013- October 2014 (comparison 2004[6,7])

Inclusion criteria: Neonates admitted in NICU during this period with seizures

Exclusion criteria: Babies with extremely low birth weight were excluded from the study

Methods

After getting Institutional Ethics Committee Approval, all neonates with seizures during the study period were included in the study. We follow neonatal protocol (SAT Hospital Protocol) sepsis screen, blood cultures, lumbar puncture if needed are done in all babies. Laboratory test like glucose, electrolytes, bilirubin, ammonia, metabolic screening, TORCH, screening are done as per protocol .Hypoglycemia was defined as sugar below 40mg/dl& hypocalcaemia as serum calcium below 7 g/dl.EEG is not routinely done for diagnosis. Cranial Ultrasonography was done using a 3.5 – 5 MHz curve probe. All ultrasonography examinations were performed from the anterior fontanels, by a single radiologist experienced in doing the procedure. If neonates continued to have seizures or had abnormal inter-ictal neurological signs, a CT or MRI examination was done later. Maternal and neonatal details were collected using a predesigned proforma and entered into MS Excel. We had compared our study with similar study done in our neonatal unit in 2004[6].The methodology and the profile are described [6,7].

Analysis

Statistical analysis was done by SPSS18 for Windows. Comparison of the proportion of neonatal seizures in two periods was compared. We also compared the clinical and etiologic profile of the neonatal seizures in two periods (2004& 2014).Results are expressed as rates and proportions.

Results

In 2014over one year, out of 3309 admissions, there were 158 neonates who had neonatal seizures. Incidence of seizures in our study was 4.77%. Out of these 44 were from inborn unit and 114 were referred from outside. Male: female ratio was 107:51(2.09:1).Term babies constituted 131cases (83%).109(68%) were of normal birth weight.37.3% presented at less than 72 hours of birth,46.2% presented between 4&7days and 16.2% presented after 7 days .Pregnancy induced hypertension was the commonest maternal risk factor(48%) followed by gestational diabetes (40.5%),PROM in 24 % and maternal Urinary tract infection in18.3%. Primigravida were 86 cases (54.6%).51.8% was born by caesarean section. Subtle seizures were the most common

seizure type found in 37 (46.25%) neonates followed by multifocal clonic seizures (42.5%).55.4% of infants had 2 or more types of clinical convulsions. None had generalized seizure.In our study only one episode of seizure was observed only in 151neonates (91.25%) while status convulsion was found in 7(8.75%).In our study, age at admission ranged from 2 hours to 10days (Mean(Sd) was 40.2hours(+or-2.54) .Term infants were affected more (83%%) compared to preterm infants (17%). The weight of neonates ranged from 1.88 to 3.98 (2.56±0.57) Kg. Out of 158 patients 32.2% were low birth weight. There was no gender difference in low birth weight.. Most (83.5%) of the neonatal seizures occurred in the first week of life. Majority (37.3%) of this were seen during initial 72 hours. First day seizures were seen in 26%, the second or third day in 39%, and rest in 3–7 days. Frequency of types of seizures was generalised tonic clonic 28%, multi focal clonic 25%, subtle 21%, focal clonic 20%, and myoclonic and focal tonic 3% each. Generalised tonic seizures were common (75%) in males while focal tonic seizures in females (67%). No significant gender difference was seen in clonic or tonic seizures (p>0.05). Subtle and Myoclonic seizures occurred more (67%) in males.

Table 1 showing comparison of clinical features

	2004	2014
Total admissions	-	3309
Mean Birth weight	-	2.56±0.57 Kg
Mean age	-	4.2(2.54)hrs
Primi mother	-	54.66%
Cesarean	-	51.8%
Prevalence of seizures	-	4.77%
Male:Female ratio	-	2.09:1
Term	-	83%
onset seizures <72hrs	96.07%	83.5%
onset seizures>7 days	3.93%	16.5%
Subtle seizures	-	46.25%
status	-	8.75%
Hospital outcome	-	3 deaths

Table 2 showing the etiology of seizures in two periods & comparison with other studies

	2004Ref6(135)N (%)	2014(158)N (%)	Comparison6,7,8 other studies
Hypoxic ischemic encephalopathy*	51(37.77%)	64(40.5%)	30-53%
Hypoglycemia*	26(19.25%)	45(28.4%)	0.1-5%
Benign neonatal seizures*	8(10.8%)	3(1.89%)	3-4%
Meningitis*	7(9.4%)	4(2.53%)	2-14%
Intracerebral hemorrhage*	5(6.7%)	13(8.22)(All preterm)	7-17%
Benign sleep myoclonus*	4(5.4%)	0	3-4%
Cerebral malformation*	3(3.6%)	5(3.165)	3-17%
Neonatal stroke*	3(3.6%)	1(0.63%)	-
Seizure disorder*	3(3.6%)	(No followup done)	-
Kernicterus*	2(2.7%)		1%
Hypocalcemia*	2(2.7%)	20(12.6%)	4.2%
Inborn error of metabolism	2(2.7%)	2(1.26%)	2%
Anoxic*	1(1.3%)	Nil	-
Unknown	6(8.1%)	8(506%)	2-10%
Multiple causes	35(25,3%%)	20(12.65%)	

*Only cause for seizures

HIE & hypoglycemia remained the common etiologies for neonatal seizures across adecade. Benign seizures were more in 2004. In our study benign seizures was not seen. Early onset hypocalcemia was high in our study (12.6%) whereas in 2004 it was 2.7%.There were 2 cases of in born errors of metabolism. In our study both were phenyl ketonuria. There were multiple causes in both studies which were comparable.

Table 3 showing relation between etiology & timing of seizures

	2004 (135)		2014 (158)	
	<72hrs	72hrs >7days	<72hrs	>72hrs
HIE	49(96.07%)	2(3.93%)	27(42.1%)	37(57.9%)
Hypoglycemia	22(86.61%)	4(15.3%)	20(45.5%)	25(55.5%)
Hypocalcaemia	3(100%)	0	18(89.9%)	2(11.1%)
Intracranial bleed	10(77%)	3(23%)	3(23%)	10(77%)
Cerebral malformation	2(66.7%)	1(33.3%)	3(60%)	2(40%)
Meningitis	2(25%)	6(75%)	2(50%)	2(50%)
Hyperbilirubinemia	1(50%)	1(50%)	1(50%)	1(50%)
Idiopathic	1(25%)	3 (75%)	1(50%)	1(505)
Others,benignseizuresetc	0	4(100%)	1	7

In 2015 study of the HIE, only 42.1% presented less than 72 hours. But 2004 study had 96.07% having reported seizures before 72 hours. Of the hypoglycemia, equal proportion presented before and after 72 hours. In early study, 86% presented below 72 hours. table 3 shows comparison in timing in two study.

In the present study neurosonogram was done in 94 cases(59.5%)Of these 73(77.6%) were reported as abnormal. The common abnormalities were periventricular leukomalacia in 24(32.8%), cerebral edema in 7cases(9.5%),ventricular effacement in 6 cases(8.2%),5(6.8%) each with intraventricular hemorrhage and cerebral malformations. . GM bleed was identified in 26 cases. Grade 1 bleed being the most common abnormality followed by grade2, 3 and 4 in decreasing order of frequency

Table 3 showing neurosonologic abnormalities

	Number(73)	%
Germinal matrix bleed	26	35.6
Periventricular echogenecity	24	32.8
Cerebral edema	7	9.5
Ventricular effacement	6	8.2
Cerebral malformation	5	6.8
HIE	4	5.4
hydrocephalus	1	1.3

Discussion

Even among trained observers, clinical neonatal seizures may be difficult to recognize and differentiate from either normal behaviors or abnormal movements of non-epileptic origin[7,8].

We had used clinical diagnosis of seizures in our study. We do not have routine video EEG for neonatal unit. In some clinical settings up to 85% of electrographic seizures are clinically silent[5].

There were 158 neonates with seizures during the study period. The incidence of seizures during study period was 4.77%.We had compared our study with similar study done in our unit 10 years back(135neonates) 2004 .[6]The etiology were similar. Mary Iypeetal had reported Hypoxic ischemic encephalopathy in 51(37.7%), Hypoglycemia in26(19.25%), Benign neonatal seizures in8(10.8%),Meningitis7(9.4%) .Table 1& 2 shows comparison of the two study

In a comparable study, out of 109 neonates the incidence of neonatal seizures in the admitted cases was 8.38%. Bangalore[8].The 50%of neonatal seizures occur on the first day, and 83.8% of all cases were seen by the seventh day.2004 study also had HIE as commonest etiology (40.5%) which was comparable to ours. Comparable (90%) occurrence was reported .[9]The early occurrence of seizures is probably due to the high occurrence of HIE in many studies.[10].The most common cause of seizure was HIE (37.9%) which was comparable with Sood A et al who reported 45.7% as due to birth asphyxia [11]. Kumar A also reported birth asphyxia as the commonest cause of seizure in first 48 hrs of life[4]. In our study 20% of the seizures were due to infections. Similar observations were reported2-14% to sepsis & meningitis [12,13,14,15.]

In our study male neonates were more in number during study period. Few other studies have reported that preponderance of male infants in the seizure population, among whom preterm infants were significantly more common[16.]In present study hypocalcaemia was observed in 11% and hypoglycemia in 20.As most of our patients were born outside details regarding antenatal and natal factors were not easily obtained. In our study one episode of seizure was observed only in 35 (43.75%) while status convulsion was found in 7(8.75%).The commonest cause for seizures was HIE (40.5%), followed by hypoglycemia (28.5%), hypocalcaemia (12.7%) and intracranial bleed (8.23%)(Table2).Another study, reported that in 48% of neonates, hypoxia was considered to be the probable main etiology, while infection and metabolic diseases including hypoglycemia and hypocalemia were next commonest causes, 12% for each condition .[17] Lien M et al, studied term early onset neonatal seizures. According to them hypoxic events contributed in 37.5%, cerebral malformations in 17.5%, cerebral infarcts in 17.5%, intracranial hemorrhages in 12.5% infections in 7.5% and unknown etiology in 7.5% .[18.19.]

Hypoglycemia was seen in 31% of neonatal seizures. This was higher than that in many other studies. This is probably due to the inclusion of out born neonates (114) who were more than inborn (44). Eriksson noted 12% as due to hypoglycemia.[19]This indicates that during neonatal transport special attention should be given to correction of hypoglycemia. Table 2 shows comparable data with other studies. Anand et al, reported from a private teaching hospital in S Kerala, that in hypoxic ischemic encephalopathy on USG revealed cerebral edema and or ischemia in 86% neonates.[21] Brain magnetic resonance imaging (MRI), computed tomography (CT) scan, and EEG, have high accuracy are not available in all neonatal units. Also it requires special conditions such as immobilization, sedation & transport.[22] Currently, ultrasonography is considered to be useful in neonatal seizures as it is safe, affordable& available at bedside.[23,24] Nabavi reported 22% neonates had neuroson-ologic abnormalities in neonates from Iran. In 2004 imaging was not widely used. As a part of prognostic study in neonatal seizures CT scan was done in 130 of 135 neonates in postnatal period. Also EEG were taken in 120 neonates. In 2015, the imaging has changed to ultrasound scan .This has been a part of protocol in many neonatal units.[25]

Conclusion

Neonates are vulnerable to seizures which is a medical emergency. Although Kerala has improved its IMR & NMR, the etiology of neonatal seiures remain same after a decade. Subtle seizures were the commonest presentation in both study. Neurosonology has become a useful investigation now when compared with previuos study.27/94 (28.72%) of neonates with seizures had neurosonologic abnormalities.

What is Known? The etiology of neonatal seizures in neonates

What this study adds? Etiology in a teaching hospital in a decadeand the neurosonologic features.

References

1. Miller SP, Weiss J Barnwell A et al. Seizure-associated brain injury in term newborns with perinatalasphyxia. Neurology 2002; 58: 542-548.
2. Calciolari G, Perlman JM, Volpe JJ. Seizures in the Neonatal Intensive Care Unit of the 1980s: Types, Etiologies, Timing. ClinPediatr (Phila). 1988 Mar 1;27(3):119–23.
3. Berg A, Jallon P, Preux P. The epidemiology of seizure disorders in infancy and childhood: definitions andclassifications. In: O Dulac et al (Eds), Handbook of Clinical Neurology. Pediatric Neurology, Part 1 (3rd edition),pp 381-398. Elsevier, Amsterdam, Netherlands, 2013.

4. Kumar A, Gupta V, Kacchawaha and Singla. A Study of Biochemical Abnormalities in Neonatal Seizure. Indian Pediatrics. 1995; 52: 424-427.
5. http://rchiips.org/NFHS/factsheet_NFHS-4.shtml accessed on 19.3.2017
6. Mary Iype, Maya Prasad, PMC Nair, S Geetha and Lalitha Kailas. The Newborn with Seizures – A Follow-up Study Indian Pediatrics 2008; 45: 749-752
7. Mayaprasad,MaryIYpe,NairPMC,GeethaS ,LalithaKailas:Neonatalseiures-A profile of the etiology & time of occurrence ,Issue2,Vol2,2011;:www.imakmj.com
8. ShahzadNajeeb, AzharMunir Qureshi, Anis-ur-Rehman, Fayaz Ahmad, Sher Shah,AsfandYar Khan*, Tahir Saeed Siddiqui AETIOLOGY AND TYPES OF NEONATAL SEIZURES PRESENTING ATAYUB TEACHING HOSPITAL ABBOTTABAD J Ayub Med Coll Abbottabad 2012;24(1http://www.ayubmed.edu.pk/JAMC/24-1/Shahzad.pdf
9. Mizrahi EM, Kellaway P. Diagnosis and Management of Neonatal Seizures (1st edition). Philadelphia,Lippincott-Raven, 1998.
10. Vasudevan c, Levene m. Epidemiology and aetiology of neonatal seizures. Semin Fetal Neonatal Med2013; 18(4): 185-191.
11. Malone a, Ryan CA, Fitzgerald a et al. Interobserver agreement in neonatal seizure identification.Epilepsia 2009; 50: 2097-2101
12. AnandNK, Gupta AK, Lamba IM. Neurosonographic abnormalities in neonates with hypoxicischemic encephalopathy. Indian Pediatr. 1994 Jul;31(7):767–74
13. Nawab T, Lakshmipathy NS. Clinical profile of neonatal seizures with special reference to biochemical abnormalities. Int J ContempPediatr 2016;3:183-8
14. Holden KR , Mellitus D and Freeman JM. Neonatal Seizures: Correlation of Prenatal and Perinatal Events with Outcome. Pediatrics. 1982; 70: 165-176.
15. Sood A, Grower N and Sharma R. Biochemical Abnormalities in Neonatal Seizure. Indian J Pediatric ; 70 (3): 221-224
16. Arpino C , Domizio S, Carrieri MP, Brescianini DS, Sabatino MG, Curatolo P. Prenatal and perinatal determinants of neonatal seizures occurring in the first week of life.J Child Neurol. 2001 Sep;16(9):651-6.
17. Doménech-Martínez E , Castro-Conde JR , Herraiz-Culebras T , González-Campo C , Méndez-Pérez: A Neonatal convulsi-ons: influence of the electroenc-ephalographic pattern and the response to treatment on the outcomeRevista de Neurologia [2003, 37(5):413-420](PMID:14533087)
18. Calciolari G, Perlman JM, Volpe JJ. Seizures in the neonatal intensive care unit of the 1980s. Types, Etiologies, Timing. ClinPediatr (Phila) 1988 Mar;27(3):119–123. [PubMed]
19. Eriksson M, Zetterström R. Neonatal convulsions. Incidence and causes in the Stockholm area. ActaPaediatr Scand. 1979 Nov;68(6):807–811. [PubMed]
20. Lien JM, Towers CV, Quilligan EJ, de Veciana M, Toohey JS, Morgan MA. Term early-onset neonatal seizures: obstetric characteristics, etiologic classifications, and perinatal care. Obstet Gynecol. 1995 Feb;85(2):163–169. [PubMed]
21. Veena Anand , P MC Nair Neonatal seizures: Predictors of adverse outcome Pediatr Neurosci. 2014 May-Aug; 9(2): 97–99.doi: 10.4103/1817-1745.139261PMCID: PMC4166859
22. Volpe, J.J. Neonatal seizures. in: J.J. Volpe (Ed.) Neurology of the

newborn. WB Saunders, Philadelphia; 2008:203–244.

23. Rowe JC, Holmes GL, Hafford J, Baboval D, Robinson S, Philipps A, Rosenkrantz T, Raye J. Prognostic value of the electroencephalogram in term and preterm infants following neonatal seizures. Electroencephalogr Clin Neurophysiol. 1985 Mar;60(3):183–196. [PubMed]
24. Seyed Saeed Nabavi, ParinazPartovi. Brain Ultrasonography Findings in Neonatal Seizure; a Cross-sectional Study. Emergency. 2017; 5 (1): e41
25. Rutherford MA, Pennock JM, Dubowitz L. Cranial ultrasound and magnetic resonance imaging in hypoxic ischaemic encephalopathy: a comparison with ˇ outcome. Developmental Medicine & Child Neurology. 1994;36(9):813-25.