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NEONATAL SEIZURES ETIOLOGICAL AND CLINICAL DIFFERENTIATION

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ABSTRACT

The fits occurring from birth to the end of neonatal period is commonly referred as Neonatal seizures; this period is one of the most important period in life time, which is susceptible for the development of seizures. The small injury in the form of mechanical malhandling to the highest genetic or congenital disorders will manifest in the form of seizures, which may become the etiology for long standing seizures. This study focuses mainly the etiological factors which may contribute for the development of neonatal seizures and clinical differentiation of the same.

KEY WORDS: Neonatal seizures, etiology, clinical differentiation.

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INTRODUCTION

A Seizure in the neonatal period is an emergency that reflects potentially significant insults to the immature brain.Seizure represent the most distinctive signal of neurological disease in the newborn period and they are the most frequent of the major manifestations of neonatal neurological disorders. It is critical to recognize neonatal seizures, determine their etiology and to treat them promptly for three reasons.

1. Seizures are usually related to significant illness, sometimes requiring specific therapy.
2. If untreated, seizures may continue for a considerable period of time and hence interfere with important measures such as alimentation or assisted ventilation.
3. Many neurological feel that seizure per se can cause brain injury.

The neonatal period is one of high seizure hazard for a number of reasons.

The last trimester and early neonatal period are characterized by rapid brain growth and development; both structure and function undergo substantial changes in a relatively short time. This process has specific metabolic demand, substarte requirements and the need to proceed under relatively ideal conditions. Unfortunately, the neonatal period is also characterized by a wide range of factors that can negatively impact this process; there are many diverse pathologic processes and disorders that may occur frequently and that may cause brain dysfunction.

In addition the relative excitability of the immature brain compared with that of older children or adults make the neonate more prone to seizure (1-6). As regards the aetiological factors in neonatal seizures they are many: some of them require multiple sophisticated investigations, while others can be diagnosed clinically with a few simple investigations. Though a few aetiological factors require sophisticated and ultramodern methods for treatment, majority of them can be treated simplistically.

Thus in present perspective, neonatal seizure deserves intensive investigation and comprehensive research. But paucity of work on this interesting filed in our country has necessitated to undertake this project.

MATERIALS AND METHODS

This study was carried out on all the neonate, who got admitted with seizure or developed seizure subsequently during hospitalization period in the Nursery of Paediatric ward ans some during routine OPD.

SELECTION OF CASES

According to Mizrahis (1) criteria all neonates with abnormal repetitive and / or stereotyped behavior were evaluated. According to Volpes (7) opinion, EEG was not considered to be a must for diagnosis of neonatal seizure cases. Cases were picked up by the history of seizure from the mothers in their neonates, and by clinical observation of ictal pattern. However following cases were excluded from the study.

1. Rapid eye movements of neonates in light sleep with closed eye and irregular respiration (Brazelton State- 2).
2. Primary apnoea of cardiorespiratory origin with concomitant bradycardia.
3. Jitteriness in newborn by observing cessation on holding the affected limbs.

METHODS

All the mothers of the neonate with seizure were carefully interviewed regarding the antenatal check up, whether they were suffering from any disease relating to pregnancy, like pregnancy induced hypertension, antepartum haemorrhage, pedal swelling, fever with or without rash, diabetes, drugs, intake, addition etc., Past obstetrics history, history of seizure during neonatal period in earlier sibling too were enquired about. Then a detailed description on present delivery particularly time of onset of labour, duration, place and mode of delivery were also enquired. Special emphasis on history taking was given on the neonate, regarding time of first cry and feeding pattern

particularly its commencement, nature and frequency. Exact time of onset seizure following birth, its pattern and presence of any abnormal behavior as noticed by the mother was also taken into consideration. Apgar score values whenever available were noted.

All the babies were weighed unclothed. Gestational age was determined form maternal history of last menstrual period by Naegill 's method. Modified Dubowitz method was used when exact history was not available. A through physical examination was carried out on all the neonates. A through physical examination was carried out on all the neonates, 48 hours after the last seizure, in naked state, under day light Special vigilance as excercised on detection of pallor, jaundice, oedema, physical malformation, cutaneous rash, naevi or vascular malformation, cataract and organomegaly. It was followed by neurological examination of the neonate when awake but not crying in Brazelton state ¾. It consisted of examination of skull and spine with head circumference cranial nerve, muscle tone and superficial, deep and primitive reflexes to find out reference of any neurological deficit.

Observed seizure pattern as noticed prior to intervention was recorded. Volpe' s(7) clinical classification of subtle, tonic, focal, clonic, multifocal clonic and myoclonic varieties with subtle variety further subdivided in to bicycling, bucconlingual, eye deviation and cyclic movement was followed.

LABORATORY PROCEDURE

Venous blood sample for haemotological and biochemical examination was collected in sterilized vials as soon as possible after the hospitalization and prior to therapy. The haematological investigation included differential WBC count, peripheral smears examination for any dsymorphic polymorphs, micro ESR and C-reactive protein estimation. The serum levels of calcium, magnesium, sodium, phosphorous and blood glucose were estimated by precipitation method, atomic absorption, spectrophotometry, flame photometry and glucose oxidase method respectively. Blood samples for culture was collected in glucose broth and after incubation for 24 hours, samples were subcultured on blood agar and Mac-conkey agar, Buffy coat smear examination, by gramstaining of buffy layer of the blood obtained after centrifugation and separation of plasma was employed for rapid identification of microorganism.

DEFINATIONS AND LABORATORY STANDARDS

Neonates born before 37 weeks were termed at preterm while those after 37 weeks as term babies. But of 42 weeks or more gestational period were nomenclatured post term. Newborn weighing between 10^{th} and 90^{th} Centile for gestation were classified as appropriate for gestational age, while those below 10^{th} centile as small for gestational age and those above 90^{th} centile as large for gestational age. Here intrauterine growth percentile chart for Indian babies as devised by Singh M. was followed. Diagnosis of Sepsis was done following Desai 1984 criteria comprised of three or more haemotological abnormalities like band cell : total neutrophil ratio >0.2, total leukocyte count < 5000, positive CRP (5mg/ ml, micro ESR > 10 mm 1^{st} hour. Meningitis was considered in cases of sepsis in the basis of low glucose, raised protein without low glucose, with or without minimal cellular response in CSF was considered as encephalitis were as follows: hypocalcemia (Ca< 7 mg/dL), hypomagnesemia (mg < 1.2 mg/dL), hypoglycemia was diagnosed if blood glucose levels were less than 30 mg/dL in term neonate and less than 20 mg/dL in preterm neonates in the first 72 hours of life and thereafter less than 40 mg/dL.

PROFORMA

A. IDENTIFICATION

1. SL. No.:
2. Regd. No.:
3. Name (B/o):

4. Sex:
5. Birth / Body Wt.:
6. Gest. Age:
7. Day of onset of seizure:
8. Type of seizure

B. HISTORY

ANTENATAL

1. Maternal Age < 18Yr. />35 Yrs.:
2. ANC from 1st trim / 2nd trim/ 3rd trim:
3. Exposure to drugs or radiation in first trim ±:
4. Mat fever during pregnancy 1st trim / 2nd trim/ 3rd trim:
5. Mat obstetrics Problem:-

APH / PIH/(Oligo/ Poly) Hydramnios.

6. Mat medical disease:

HTN/DM/Renal disease / ITP

7. Mat habits:

Smoking / Alcoholic / Narcotic.

8. Past H/o neonatal seizure in sibs.

NATAL

1. Place of delivery: Home / Hospital.
2. Second stage: Prolonged / Precipitate delivery.
3. Premature rupture of membrane: ±
4. Meconium staining of liquor : +/-
5. Presentation : Breech / Face / Brow.
6. Method of delivery:

V.D/ V.E./L.A/ Forceps/ C.S..

IMMEDIATE POSTNATAL PERIOD

1. APGAR score.
2. First feed : Early / Delayed.
3. Frequency of feeding : Frequent / infrequent.
4. Feed : Breast milk/cows milk/Artificial milk/plain water / None.

C. EXAMINATION

General Examination:

1. Posture : Flexion/Extension/ Intermediate.
2. Activity: Poor / Good.
3. Cry: Depressed / High Pitch / Week / Normal.
4. Colour : Pallor / Jaundice / Cyanosis / Pink.
5. Respiratory Rate:
6. Heart Rate
7. Head Circumference
8. Cranial deformity Caput / Moulding / Cephalhematoma.
9. Facies : abnormal / normal.
10. Chest.
11. Abdomen : Distended / Scaphoid.

Umbalicus : Health / Discharge

Heapatosplenomegly: ±

Genitalia Normal / Abnormal
12. Extremities

D. Neurological Examination

1. Preliminaries, Last feeding State.
2. Cranial nerves
3. Motor System

Tone and Posture : Hypertonic / Hypotonic / Normal.
Tendon reflexes : Increased / decreased / Normal.
Abnormal movement : Jitteriness / Seizure.

4. Sensory System Normal / Abnormal.
5. Neonatal relflexes :

Moro's Reflx Sym / Asym/ Dep/ Exagg.
Tonic neck: Momentary / Presistent
Palmar and Plantar grasp : Strong or weak
Rooting & Sucking : weak / strong.
Placing & steeping : Absent / Exaggerated / Normal.

E. INVESTIGATION

Biochemical

1. Blood Glucose –
2. Serum Calcium
3. Serum magnesium
4. Serum Phosphorous-
5. Serum Sodium

Septic workup

1. D.C. of WBC – Band cell: Mature neutrophil
2. TLC
3. M-ESR
4. CRP
5. Blood culture -+/-
6. CSF

Cytology
Biochemical : Sugar / Protein
Culture

Special investigation

1. EEG
2. USG

RESULTS

This piece of study was undertaken in patients admitted to the Department of Pediatrics, M.K.C.G. Medical College Hospital, Berhampur during the period of August, 2011 to July 2012. The following are the observations and analysis of this study.

TABLE –1

Distribution of various etiology among preterm and term Neonates.

Etiology	Pre – term		Term		Total	
	No.	%	No.	%	No.	%
HIE	7	19.40	29	80.50	36	100.00
Primary ICH	6	85.00	1	14.20	7	100.00
Infection						
i) Meningitis	3	33.33	6	6.66	9	100.00
ii) Septicaemia	4	66.66	2	33.33	6	100.00
Primary Metabolic						
i) Hypoglycemia	3	30.00	7	70.00	10	100.00
ii) Hypocalcemia	2	18.18	9	81.81	11	100.00
iii) Hyponatraemia	2	100.00	--	--	2	100.00
Kernicterus	2	66.66	1	33.33	3	100.00
Malformation	1	50.00	1	50.00	2	100.00
Heaomorrhagic	0	0.00	1	100.00	1	100.00
Unknown	3	30.00	7	70.00	10	100.00
Total	33	36.66	57	63.33	90	100.00

Note: 7 term babies had shown hypoglycemia and hypocalcemia simultaneously.

Table 1 reveals that out of total 90 cases of neonatal seizures studied, 36 were due to HIE and 7 due to primary ICH. Kernicterus, malformations and hemorrhagic disease of newborn each had constituted 3,2, and 1 cases respectively. Out of 15 cases of infective origin, 9 had meningitis and 6 had septicaemia. Hypoglycemia, hypocalcemia and hyponatremia was seen in 10, 11 and 2 cases respectively, Neither isoloated hypomagnesemia nor hypernatremia was found to be cause of neonatal seizure in any on the neonates under study. No neonate had responded to trial of pyridoxine which it was administered to refractory seizure could not be determined in 10 neonates. The ratio of preterm to term was 33:57 indicating that term babies are more prone to seizure. No neonates with seizure was born at or after 42 weeks of gestation.

Table – 2

Day on onset of seizure in different etiological categories

Etiology	DAYS OF PRESENTATION						
	1	2	3	4-7	8-14	15-28	Total
HIE	18	14	4	--	--	--	36
Primary ICH	1	3	2	1	--	--	7
Infection	2	--	1	1	9	2	15
Hypoglycemia	1	5	3	1	--	--	10
Hypocalcemia	1	4	2	3	1	---	11
Hyponatraemia	1	--	1	--	--	--	2
Kernicterus	--	--	1	2	--	--	3
Malformations	1	--	--	--	--	1	2
HDN	--	--	--	--	--	1	1
Unknown	2	5	--	3	--	--	10
Total	27 (30%)	31 (34.4%)	14 (15.5%)	11 (12.2%)	10 (11.11%)	4 (44.4%)	90 (100.00%)

Table 2 shows that except in 14 cases, seizure began within the first week of life. In rest of the neonates, 18 cases of HIE had seizure onset on the first day, 14 on second day and 4 cases on third day. Primary ICH had given rise to seizure on 3 cases on second day, and 2 cases on third day and 1 cases each on first day and in between fourth to seventh day period. Early onset hypocalcemia occurred in 4 cases on second day of total 7 cases with first 3 days. 2 cases had seizure on first day due to early neonatal infection.

Table – 3 (i)
Caused of Seizure of Relation to Antenatal Check up of Mothers

Etiologies	ANCs in Trimester			
	0	1	2	3
HIE (36)	14	4	7	11
ICH (7)	1	1	4	1
Hypoglycemia (10)	0	0	4	6
Early Hypocalcemia (7)	0	0	2	5
Late Hypocalcemia (4)	3	0	0	1
Hyponatraemia (2)	0	0	1	1
Early Infection (5)	5	0	0	0
Late Infection (10)	0	0	8	2
Kernicterus (3)	3	0	0	0
Malformation (2)	1	0	1	0
HDN(1)	1	0	0	0
Unknown (10)	0	5	5	0
Total (90)	28	10	30	22

Table – 3 (ii)
Causes of seizure in Relation to Meternal diseases, Place and mode of delivery

Etiologies	Maternal Disease		Place of Delivery		Mode of Delivery			
	+ve	-ve	Hosp.	Out	VD	VE	FE	CS
HIE (36)	26	10	14	22	16	3	6	11
ICH (7)	09	1	5	2	6	1	0	0
Hypoglycemia (10)	9	1	1	9	3	2	5	0
Early Hypocalcemia (7)	7	0	0	7	0	2	5	0
Late Hypocalcemia (4)	0	4	0	4	2	2	0	0
Hyponatraemia (2)	2	0	0	2	2	0	0	0
Early Infection (5)	4	1	0	5	5	0	0	0
Late Infection (10)	2	8	3	7	2	5	0	3
Kernicterus (3)	3	0	0	3	2	1	0	0
Malformation (2)	1	1	1	1	1	1	0	0
HDN(1)	0	1	0	1	1	0	0	0
Unknown (10)	3	7	7	3	5	2	0	3
Total (90)	56	34	31	59	45	17	11	17

The above table 3(i) and (ii) shows antenatal status of mother of seizure babies. 10, 32 and 27 had done antenatal check up from 1st, 2nd and 3rd trimester onwards, while 28 mothers had not taken any form of antenatal care. Maternal ailment associated with neonatal seizure was recorded in 63 cases. Only 31 deliveries occurred in this hospital, rest 66 (VE), forceps extraction (FE) and caesarean section (CS) constituted 45, 19, 16 and 17 cases respectively.

Table – 4
Feeding pattern among neonates with seizures

ETIOLOGY	First Feed		Frequency		Feed				
	Timely	Delayed	Frequent	Infrequent	Breast Milk	Cow's Milk	Artificial Milk	Plain water	Nothing Orally
HIC (36)	10	26	2	34	4	1	3	2	26
ICH (7)	2	5	1	6	3	--	1	1	2
Hypoglycemia (10)	--	10	--	10	1	--	1	4	4
Early Hypocalcemia (7)	--	7	--	7	1	--	1	3	2
Late Hypocalcemia (4)	4	--	4	--	--	4	--	--	--
Hyponatraemia (2)	--	2	--	2	--	--	--	1	1
Early Infection (5)	2	1	--	3	1	--	1	1	--
Late Infection (10)	47	8	3	9	1	3	8	--	--
Kernicterus (3)	1	2	--	3	1	--	--	--	2
Malformation (2)	1	1	1	1	1	--	--	1	--
HDN(1)	--	1	--	1	--	--	1	--	--
Unknown (10)	5	5	6	4	5	1	2	2	--
Total (90)	29	61	17	73	17	9	17	12	35

From The above table it is evident that 29 babies were timely fed while rest 61 were lately fed. Only 17 were properly fed while rest 73 were infrequently fed. Feeding of breast milk, cow's milk, artificial milk and plain water were to 17, 9, 17 and 12 babies respectively. 35 babies were given nothing orally till the time of onset of seizure. As malformations, kernicterus and seizure due to unknown causes showed no biochemical alternations they had been deleted from the observation table.

Table- 6
Different clinical patterns associated with different etiologies of Neonatal seizure

Etiology	Subtle	Multifocal clonic	Focal clonic	Myoclonic	Tonic	Total
HIE	12 (33.3%)	5 (13.8%)	9 (25.0%)	7 (19.4%)	6 (16.6%)	36 (100%)
ICH	5 (33.3%)	1 (14.2%)	--	2 (28.5%)	4 (57.1%)	7 (100%)
Meningitis	4 (44.4%)	5 (55.5%)	2 (22.2%)	2 (22.2%)	2 (22.2%)	9 (100%)
Specticaemia	4 (66.6%)	2 (33.3%)	2 (33.3%)	--	--	6 (100%)
Hypoglycemia	9 (90.0%)	1 (10.0%)	5 (50.0%)	--	5 (30.0%)	10 (100%)
Early Hypoglycemia	1 (14.2%)	1 (14.2%)	2 (28.5%)	--	3 (42.8%)	7 (100%)
Late Hypocalceima	--	4 (100.0%)	--	--	--	4 (100%)
Hyponatraemia	1 (50.0%)	--	2 (100.0%)	--	--	2 (100%)
Kernicterus	2 (66.6%)	1 (33.3%)	1 (33.3%)	--	--	3 (100%)
Malformation	--	--	--	1 (50.0%)	1 (50.0%)	2 (100%)
HDN	--	--	1 (100.0%)	--	--	1 (100%)
Unknown	2 (20.0%)	2 (20.0%)	5 (50.0%)	1 (10.0%)	--	10 (100%)
Total	40 (44.4%)	28 (24.4%)	29 (32.2%)	13 (14.4%)	19 (21.1%)	90 (100%)

Subtle, mutifocal clonic, focal clonic, myoclonic, tonic patterns were observed in 40, 22, 29, 13 and 19 cases respectively. Maximum number of subtle and clonic seizures occurred in Hypoxic – Ischemic encephalopathy group. Meningitis and late onset hypocalcemia presented predominantly as multifocal clonic seizures.

Table – 7
Distribution of Different clinical types of neonatal seizures in preterm and term neonates

Clinical Type	Preterm (n-33)		Term)n=57)	
	No.	%	No.	%
Subtle	26	78.78	14	24.50
Mutlifocal clonic	2	6.00	20	35.00
Focal clonic	14	42.42	15	26.30
Myoclonic	11	33.33	3	5.20
Tonic	8	24.24	11	19.20

Table 7 shows subtle seizure as the commonest form of seizure in preterm babies, Multifocal clonic is the commonest variety of seizure in term neonates, it was observed in 20 term neonates. Myoclonus was observed mostly in preterm babies, clonic as well as tonic seizures had been almost equally distributed among preterm and term babies.

Table – 8
Course of Neonatal Seizure cases during Hospital Stay in relation to etiologies

Cases	Normal	Died	Recurrent Seizures	Neurological deficit	Total
HIE	12 (33.3%)	12 (33.3%)	10 (27.2%)	12 (33.3%)	36 (100%)
ICH	2 (28.5%)	3 (42.8%)	2 (28.5%)	2 (28.5%)	7 (100%)
Infection	5 (33.3%)	5 (33.3%)	3 (20.0%)	5 (33.3%)	15 (100%)
Hypoglycemia	8 (80.0%)	2 (20.0%)	---	--	10 (100%)
Hypocalcemia	10 (90.9%)	1 (20.0%)	--	--	11 (100%)
Hyponatremia	2 (100%)	--	--	--	2 (100%)
Malformations	--	1 (50.0%)	1 (50.0%)	1 (50.0%)	2 (100%)
Kernicterus	--	1 (33.3%)	1 (33.3%)	2 (66.6%)	3 (100%)
HDN	1 (100.0%)	--	--	--	1 (100%)
Unknown	8 (80%)	2 (20.0%)	---	--	10 (100%)
Total	41 (45.5%)	27 (30.0%)	17 (18.8%)	22 (24.4%)	90 (100%)

Table 8 shows that out of 90 neonates with seizures 41 cases recovered and were normal at the time of discharge. While 22 were left with some neurological deficit. 27 neonates with seizures expired while 17 exhibited recurrent seizure during hospitalisation period.

DISCUSSION

Hyoxic ischemic encephalopathy was found to be the commonest cause of neonatal seizure had in this study (Table 1), with 36 out of total 90 cases of seizure had hypoxic-ischaemic encephalopathy and thus HIE was responsible for neonatal seizures in 40 % of total cases. This is similar to the findings of Kumar et al. (8) where 45 of neonatal convulsions were due to HIE. The higher percentage of HIE in Indian studies may be due to higher prevalence of risk factors for birth asphyxia in developing countries than in developed countries. Women in developing countries have poor health and the risk of pregnancy and delivery complications in these women in high. Incidence of primary Intracranial haemorrhage, infection, primary metabolic causes are 8%, 17% and 18% respectively as they had constituted 7, 15 and 16 cases respectively. Brown et al (6) had recorded them in 50%, 26% and 16% in his series. The low incidence of ICH cases in this study was due to exclusion of secondary of secondary causes by birth asphyxia. Again, occurrence of hypoglycaemia, hypocalcemia and hyponatremia were recorded in 10 (62%) , 11 (68%) and 2 (12%) instances out of total 16 cases with primary metabolic alternation. In this group 7 babies had shown simultaneous occurrence of both hypoglycaemia and hypocalcemia. This is similar to observation of Kumar et al (8), where hyponatremia occurred in 10% cases while hypoglycaemia and hypocalcemia both occurred in 55% of his cases. In the neonatal seizure group of infection origin 9 cases (60%) were due to meningitis while the rest 6 cases (40%) were caused by septicaemia. Malformation and Kernicterus had low incidence of 2.2% and 3.3% and 2 and 3 cases respectively. No case of seizure due out either narcotic withdrawal or accidental injection of local anaesthetic into fetal scalp had been recorded as those practices being distinctly uncommon in mothers in this region. The exact cause remained undetermined in 10 (11%) cases which correlates well with Mizrahi (1) series which showed 9% cases with undetermined cause. Among them no case had a family history of neonatal seizures which rules out possibility of benign familial convulsions. 2 cases among the above group had intractable seizures and expired which did not respond to pyridoxine infusion. These cases could be one of inborn error of metabolism, which could not be identified because of lack of facilities. No cases of seizure showing hypertremia nor hypomagnesemia was detected. Seizure had occurred in 33 (36.6) preterm as against 57 (63.6%) term neonates. No baby with seizure had gestational age of 42 weeks or more. This corroborates well Goldberg et al (9) study revealing 34% of neonatal seizure affecting the preterm babies.

However detailed analysis of relative frequency of each etiology among preterm and term neonates (Graph- I) showed that preterm babies had dominated over 3 sectors Viz. ICH (86%), Hyponatremia (100%) and kernicterus (66%). The common occurrence of ICH in preterm was attributed to their richly vascular source of organ from capillaries in the subpendymal germinal matrix, more pronounced in fetus of 6-8 months of gestation . Frequency of Kernicterus in preterm was explained by increased bilirubin transport across immature blood brain barrier in them.. The time of seizure onset and etiology may be related (Volpe, et al)(10). Some etiologies may causes seizures throughout the neonatal period. Other factors, such as hypoxia-ischemia, hemorrhage and some metabolic disturbance, may be associated with seizure in the first week of life, whereas infection and other metabolic disturbance may cases seizure later (1). The peak incidence of seizure occurred on the second day of life. 31 neonates had seizure on the 2nd day which was 34% of the total (Table 2). Rose et al (11) had also found the highest occurrence of neonatal seizure on the 2nd day (33% cases). Most of the cases of HIE induced seizure (88%) cases were observed on first two days with maximum number (50%) on the very first day. This correlates well with 50% of cases

of HIE on 1st day by Rose et al (11). Convulsions the HIE, ICH cases were well confined within 1st week with the peak on the on the second day. The second day peak is also seen in hypoglyceamia and hypocalcemia of early onset with 50% and 57% cases respectively. Rose et al (11) to observed that hypoglycaemia had its peak on the second day with 3/7 cases. Among early onset and late onset infection cases maximum incidence of seizure occurred on 1st day and 2nd week respectively, the respective figures being 66% and 75%. Graph -2 depicts bimodal distribution pattern of neonatal seizures due to hypocalcemia and neonatal sepsis, comprising both early and late onset varieties. HIE cases had shown their peak on the very first day followed by a sharp descent after the second day. Hyponatremia cases were confined within the first 72 hours of life. Rest of the causes showed scattered distribution pattern.

Table 3 shows relative proportion of seizure as 31:59 among babies born inside hospital and born outside hospital. Again only 17 were delivered by vaginal delivery with episiotomy while 45 were delivered vaginally without episiotomy rest 11 and 17 cases were delivered by forceps and by caesarean section respectively. Thus quite a high proportion of mothers had not received good intrapartum care. Surprisingly only 10 mothers availed antenatal care from trimester onwards while 30 and 22 members availed antenatal care from 2nd and 3rd trimester onwards. 28 mothers did not receive any antenatal care. This low rate of proper antenatal care of pregnant mothers had resulted in higher incidence of maternal diseases and complicated deliveries mostly outside hospital, ultimately producing seizures in their babies. These results correlate with Bharadwaj et al (4). He found ignorance illiteracy, poverty and lack of faith in modern system of medicine to be responsible for poor maternal care receptivity. Feeding pattern analysis of neonates with seizures (Table 4) shows that the first feed was delayed in 61 cases and 73 babies were improperly fed. Breast milk, cow's milk and artificial milk were offered to 17, 9 and 17 babies respectively while 10 were on plain water. Nothing was given orally due to factors, in one group VIZ HIE babies were too sick to be fed orally, so parental nutrition was offered to them. In the second group, lack of proper conception about breast feeding among mothers had resulted in seizure among their neonates. The feeding, pattern of all the babies with hypoglycaemia and early onset hypocalcemia was totally erratic with delayed and infrequent feeding to all of them. This finding was analogous to similar observations in Indian study by Kumar et al (8) who came across 2 neonates with simultaneous hypoglycaeima and hypocalcemia out of total 35 neonates, fed infrequently. All the neonates with late onset hypocalcemia were on cow's milk. Similar observations was made by Kumar et al (8).

Secondary biochemical alteration in primary causes of seizure (Table 5 were recorded in 18/36 (50%); 4/7 (57%); 5/9 (56%) and 1/6 (17%) cases of HIE, ICH, Meningitis and septicemia respectively. Hypocalemia with or without hypomagnesemia and hyperphosphotemia occurred in 4/36 (11%) cases of HIE and was in close correlation with findings from western literature by Erikson et al (14) with 12.5% case. This is attributed to transient functional hypoparathyroidism, increased phosphate load and bicarbonate therapy (Tsang et al (12). Hypoglycemia was observed in 8/36 (22%, 1/7(14%), 1/9 (11%), 1/6 (16.6%) cases of HIE, ICH, Meningitis and septicemia. Hypoglycemia in seizuring babies with infective aetiologies were attributed to inadequate intake and increased metabolic rate . Hyponatremia was observed in 10/36 (27%) , 3/7 (43%), 4/9 (44%) case of HIE ICH and meningitis respectively. Similar observation was made by Kumar et al (8) and it was attributed to the syndrome of inappropriate antidiuretic hormone secretion in sick babies. Table 6 shows that HIE and meningitis were associated with all forms of seizure patterns. In HIE focal clonic and subtle varieties of seizures were commonly observed, they constituted, 9/36 (25%) and 12/36 (33%). Rest constituted as myoclonic 7/36 (19.4%), tonic 6/36 (16.6%) and multifocal clonic 5/36 (14%) cases. This was in

accordance with earlier observations made by Brown and Minns (13). In ICH subtle seizure was commonest clinical pattern with incidence of 5/7 (71%) cases followed by tonic seizure in 4/7 (57%) cases. Hypocalcemia of early and late onset varieties showed nultifocal clonic in 5/11 (45%) and tonic in 3/11 (27%) predominantly. Over all analysis ,revealed that subtle seizure was the commonest clinical pattern seen in 40/90 (44) cases and was in close correlation with similar findings by Scher(1989) who found it in 33% of cases. Multiple types of seizure pattern was commonly seen in many babies. Mizrahi and Kellaway et al (1) has observed that 22% of neonates with seizures experienced more than one type of seizure. Table – 7 reflected that subtle an myoclonic pattern were more commonly seen among preterms compared to term babies with relative incidence of 26/40 (65%) and 11/14 (80%) respectively. This was in accordance with that of Scher, 1989. Focal clonic and tonic seizurs are seen equally in preterm and term neonates multifocal clonic seizure were commonly seen in term neonates. Limited period of follow up, prior to discharge showed that (table 8) infection HIE and were two most leading cause of death in neonates with seizures in this study with 44% and 18% cases respectively. Indian study by Bharadwaj et al (4) had also found these two factors to be most important derterminant of neonatal mortality. Neurological deficit were mostly detected among babies with HIE (55%) while most of the seizure babies who become normal at the time of discharge were in hypocalcemic group (90%). All these observations were similar to the observations by Rose (1970). Recuurences of seizure were most frequent in HIE group.

CONCLUSION

In the present study of 90 neonates with seizure, 33 (36%) were preterm while rest 57 (63.33%) were term babies. HIE was the commonest causes of seizures present in 36 cases (40%). The frequency of other causes were, primary I.C.H, infection, primary metabolic disturbances and malformation in 8%, 17% , 18% and 2.2% cases respectively. The exact cause remained undetermined in 11% cases. Relative frequency of hypoglycemia, hypocaclemia, hyponatremia cases were 62%, 68% and 12.5% respectively. No seizure of pyridoxine dependency primary hypomagnesemia, hypernartermia origin was found. ICH, hyponatremia and Kernicterus cases were seen mostly in preterm with relative frequency of 86%, 1000% and 66% respectively. Most of the seizure (34%) occurred on second day. The peak incidence of seizure caused by HIE and early sepsis were on the first day with 46% and 66% cases respectively. Seizure in neonates born outside hospitals outnumbered the neonates born inside hospitals by 59 to 31 cases. They were mostly delivered by vaginal route without episitomoy despite maternal problems requiring institutional delivery. Only 10% mothers had undergone complete antenatal check up in the study group. Delayed and infrequent feeding were observed in 61 and 73 cases respectively while only 17 were breast fed. But all the hypoglycemic and early hypocalcemia cases had totally erratic feeding pattern. All the late hypocalcemia cases (4) were solely on cow's milk. Secondary biochemical abnormalities had occurred in 18(50%) , 4 (57%), 5 (55%) 1 (16%) cases of HIE, ICH, meningitis and septicemia respectively. The incidence of hypoglycemia hypocalcemia and hyponatremia in HIE cases were 8, 4 and 10 cases respectively. Most frequent type of seizure observed was subtle variety. Meningitis, HIE cases had showed all patterns of seizure Viz. Clonic , subtle myoclonic, tonic and multifocal clonic. Other common pattern being subtle in ICH (71.0%) and hypoglycemia (90%). Tonic in early onset hypocalcemia and multifocal clonic in (100%) late onset hypcalcemia.

Leading causes of death were infection 5/15 (33.3%) and HIE 18/36 (33.3%). Highest percentage of neurologic deficit was seen in Kernicterus cases (66.6%) while complete recovery was seen in cases of seizures due to hypocalcemia (90%) . HIE remained most frequent cases of recurrent seizures (27%).

Based on the observation though HIE with secondary biochemical abnormalities was the commonest direct cause of neonatal seizure, it is clear that poor antenatal and natal maternal care being the single most important indirect factor for neonatal seizure. It is felt essential to generate awareness among the pregnant mothers through constant health education, so that mothers become receptive to the basic "Primary health care " services being provided to them during pregnancy and delivery and for improvement of infrastructures and referral system for quality natal and immediate neonatal care by trained medical and paramedical personnel. In addition, to bring down the high incidence of primary metabolic abnormalities as another important cause of neonatal seizure, promotion of early and exclusive breast feeding through adoption of baby friendly hospital policy. Moreover practice of early rooming in will possibly allow early clinical diagnosis of seizure by the mother themselves.

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