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Original Research Article

An Observational Study on Clinico-Etiological Profile of Neonatal Seizures

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ABSTRACT

Background: Neonatal seizures are the most common neurological emergencies encountered in newborns. Neonatal seizures are poorly classified, under-recognized and often difficult to treat. The present study is aimed to find out the spectrum of causes of neonatal seizures with its relationship to various parameters like gestational age, etiology, seizure type.

Material and methods: This Hospital based observational, cross-sectional study was conducted in the level-II Neonatal Intensive Care Unit of Department of Pediatrics, Jawaharlal Nehru Hospital and Research Centre Bhilai, Durg, Chhattishgarh for One year (December 2019 – November 2020). Sample size was 110[3, 4, 5]. The parents of admitted newborns were approached and consent was taken. Study subject were selected as per above mentioned inclusion and exclusion criteria. All cases included in this study were evaluated on following parameters-History, Physical Examination & Measurement of laboratory parameters.

Results: The above table shows the detailed demographic details of our study group in relation to sex, maturity and birth weight. Amongst our 110 subjects with seizures, we had a total number of male neonates in our study were 61 (55.45%), and female neonates were 49 (44.55%)

Conclusion: Our incidence of neonatal seizures in hospitalized NICU was3.32%. The male to female ratio in our study was 1.2:1. The most common cause of neonatal seizures in our study was birth asphyxia, followed by metabolic abnormalities. This was followed by meningitis. Birth asphyxia was the most common cause of seizures in preterm cases. The metabolic abnormalities (hypoglycemia, hypocalcemia and hypernatremia) were the most common cause of seizures in term neonates.

Keywords: Seizure, Tonic, Clonic, Myoclonic, Generalized

INTRODUCTION

Neonatal seizures are the most common neurological emergencies encountered in newborns. Seizure is defined as a hyperexcitation in neurologic function, i.e., motor, behavior and / or autonomic function. Neonatal seizures are overt manifestations of neurological dysfunction. Neonatal seizures have been neglected for years, so it is difficult to classify and treat as very less literature is available. Neonatal seizures present with varying manifestations like

generalized, tonic, multifocal, clonic, myoclonic and subtle activity. As per the literature available, Incidence in pre term neonates (20.8 per 1000 live births) more than term neonates (8.4 per 1000 live births).[1] overall of Neonatal Seizure incidence is found to be 10.3 per 1000 in live birth.[1] Infants with Neonatal Seizure are at high risk of neonatal death or neurological impairment and epilepsy disorders in later life. Over the period of time there is decrease in mortality as a consequence of neonatal seizure from 40% to about 20%, but still there is no effect on its long-term neurodevelopment sequelae i.e., 30 %.[2] The presence of neonatal seizures indicates an underlying ominous neurological condition, most commonly hypoxic-ischemic insults. Stroke, intracerebral hemorrhage, meningitis, sepsis and metabolic disorders are the other risk factors of neonatal seizures. There Several mechanisms may which adversely affect the growing and developing brain of neonates during this period; some of these conditions are as: hypoxia, ischemia, infections, inflammations, malformations, maternal drug abuse, coagulative disorders and postpartum injuries to neonate.

Taking above points into consideration, this study was planned to know the etiology. The present study is done at a level-II NICU of institute in town place of Bhilai city of Chhattisgarh state. The present study is aimed to find out the reasons of neonatal seizures with its relationship to various parameters like gestational age, etiology, seizure type.

MATERIAL AND METHODS

This Hospital based observational, cross-sectional study was conducted in the level-II Neonatal Intensive Care Unit of Department of Pediatrics, Jawaharlal Nehru Hospital and Research Centre Bhilai, Durg, Chhattishgarh for One year (December 2019 – November 2020). According to literature studies, the neonatal seizure incidence found to be ranged from 0.1-0.5% in Term neonates and 10-22.7% in Preterm neonates.[3, 4, 5]
Sample size formula -[6]$n=4pq/L^2$.
So, we will take around 110 sample size.

Inclusion Criteria:

1) Neonates presenting with any clinical type of seizures (generalized tonic, multifocal clonic, focal clonic or myoclonic seizures) with or without subtle motor and autonomic manifestation will be included in the study group.

2) Those neonates whose parents have given consent.

Exclusion Criteria:

Neonates with Jitteriness, Tetanic spasms in neonates, Neonates with benign sleep myoclonus & Neonates whose parents or caretakers did not give consent.

Ethical clearance was obtained from Institutional ethical committee. Informed and written consent of parents was taken. The parents of admitted newborns were approached and consent was taken. Study subject were selected as per above mentioned inclusion and exclusion criteria. All cases included in this study were evaluated on following parameters.-History(demographic details and detailed antenatal history **(**mothers age, gestational age, birth order) ,intra natal history (prolonged or difficult labour, birth asphyxia, sepsis) , h/o diabetes mellitus, and h/o drug consumption during pregnancy), Physical Examination (examination of vitals, 4 limbs BP, cyanosis, looking for associated malformations/ syndromes, and systemic examination of all the major organ systems, anthropometric measurements to look for macro/microcephaly) & Measurement of laboratory parameters. Following baseline investigations were done appropriately in our study cases -CBC & hemogram, Blood culture, Biochemical profile – serum calcium, serum electrolytes and blood sugars examination, ABG analysis (Arterial blood gas), pulse oximetry monitoring, USG skull, fundus examination, Neuroimaging findings, EEG, inborn errors of metabolism work up depending on the likely diagnosis & BOA/BERA Following standard definitions and working threshold levels were considered while enrolling neonates with convulsions.

A seizure in neonate was defined as:

(a) subtle seizure if neonate had jerking of eyes, blinking or fluttering of eyelid, staring look, sucking, chewing or smacking Oro- buccal movements or apnoeic attack.

(b) Multifocal clonic seizure if neonate had clonic convulsive movements migrating haphazardly from one limb to another.

(c) Focal Clonic seizure if the neonate had a well localized clonic convulsion.

(d)Tonic seizure if, the neonate had generalized stiffening associated with stertorous breathing and occasional clonic jerks.

(e) Myoclonic seizure when the neonate had sudden jerky movements.
Standard N.I.C.U protocols was followed for management of all cases for their underlying condition in an actively convulsing neonate.

Data Analysis:

After data collection in predesigned & pretested proforma, data entry was done in Excel. Data analysis was done with the help of SPSS Software ver. 23 trial. Qualitative data is presented with the help of Frequency and Percentage table, association among study group is assessed with the help of Chi-Square test. P value less than 0.05 is taken a significant level.

RESULTS

The study "To Study the Clinico-etiological Profile of Neonatal Seizure Hospital & Research Centre (C.G.) At Level-II Newborn Intensive Care Unit" was a hospital based, observational, conducted on the newborns admitted in level II NICU from December 2019 to November 2020 in the Department of Paediatrics, JLN. Total 110 newborns with seizure were enrolled in this study. The data was collected, analyzed and observations in form of tables are as follows:

Table-1: Demographic Profile of Study Group

Study factors		Frequency	percentage
Gender	Male	61	55.45
	Female	49	44.55
Gestation	Full term	86	78.18
	Preterm	22	20
	Post term	2	1.82
Weight (Kg)	Less than 1.5	2	1.82
	1.5 to 2.5	32	29.09
	More than 2.5	76	69.09
	Total	110	100.0

The above table shows the detailed demographic details of our study group in relation to sex, maturity and birth weight. Amongst our 110 subjects with seizures, total number of male neonates in our study were 61 (55.45%), and female neonates were 49 (44.55%). Also, the table reveals that the total number of full-term neonates were 86 (78.18%), preterm 22 (20%) and 2 (1.82%) were post term neonates. Most neonates 76 (69.09%) in study were in more than 2.5 kg birth weight followed by neonates 32 (29.09%) have birth weight 1.5 kg to 2.5 kg and 2 (1.82%) neonates are in less than 1.5 kg birthweight.

Table-2: Etiology of Seizures in the Study Group

Etiology	N	%
Birth Asphyxia	49	44.55
Hypoglycemia	17	15.45
Hypocalcemia	18	16.36
Hypernatremia	7	6.36
Cerebro vascular	3	2.73
Hypoxia	2	1.82
Meningitis	7	6.36
NN Hyperbilirubinemia	2	1.82
5th Day Seizure	1	0.91
Unknown	4	3.64
Total	110	100

The above table shows that the cause having highest no. of neonatal seizures in our study was Birth asphyxia accounting for 49 (44.55%) cases, followed by metabolic cause in 42 (38.18%) cases (including hypocalcemia, hypoglycemia, hypernatremia). This was followed by Meningitis in 7 (6.36%) cases and 3 (2.73%) cases of cerebrovascular, hypoxia. There were 4 (3.64%) cases of which cause is unknown. There were 2 (1.82) cases of hypoxia and NN Hyperbilirubinemia. 5th Day seizure account for 1 case (0.91%).

The most common metabolic cause of seizures was hypocalcemia in 18 (16.56%) cases. There were 17 (15.45%) cases of hypoglycemia while 7 (6.36%) cases of hypernatremia. 3 cases of Cerebrovascular causes were there, out of which 1 case was due to Subdural haemorrhage and 2 cases were due to Intracerebral haemorrhage. Among all other causes, 2 cases of hypoxic convulsion were cases of complex cyanotic heart disease whereas 4 cases remain undiagnosed hence considered under unknown etiology.

Table-3: Spectrum of Seizure Types

Seizure Type	Frequency	Percentage
Clonic	20	**18.18**
Tonic	26	**23.64**
Myoclonic	4	**3.64**
Subtle	60	**54.55**
Total	**110**	**100.0**

In our study, the most common type was Subtle type of seizures accounting for 60 (54.55%) cases, followed by Tonic type accounting for 26 (23.64%) cases and Clonic type of seizures in 20 (18.18%) cases. Myoclonic type accounted for only 4 cases (3.64%) in our study.

Table-4: Comparison between Type of Clinical Seizures and Gestation

Gestation period	Seizures				
	Clonic	Tonic	Subtle	Myoclonic	Total
Preterm	5	4	13	0	22
%	26.32	15.38	21.67	0	20.18
Term	13	22	47	4	86
%	63.16	(84.62	78.33	100	77.98
Post term	2	0	0	0	2
%	10.53	0	0	0	1.83
Total	19	26	60	4	110
	100	100	100	100	100

(Chi-square test = 11.93, DF = 6, P value = 0.063, not Significant) In our research, out of total 110 cases of seizures, 85 (77.99%) cases occurred in full term, 22 (20.18%) cases in preterm and 2 (1.83%) cases in post term. Amongst these cases 60 (55.45%) were of Subtle type, in which 47 (78.33%) cases were in full term, 13 (21.67%) cases were in preterm.

This was followed by tonic seizure type occurring in 26 cases (23.63%), in which 22 (84.62%) in full term and 4 (15.38%) in preterm.

The statistical analysis was not significant though numerically significant and therefore we could not ascertain a particular type of seizure that is more common at a particular gestational age.

Clonic seizure type followed the above seizure types occurring in 19 (17.27%) cases out of which 12 (54.54%) full term neonates, 5 (26.32%) preterm and 2 (10.82%) post term neonates.

There was only 4 case of myoclonic seizure which occurred in full term neonate.

Table-5: Association between Etiology and Clinical Seizure Type

Etiology	Seizures				
	Clonic	Tonic	Subtle	Myoclonic	Total
Birth Asphyxia	6	16	26	1	49
%	12.24	32.65	53.06	2.04	100
Hypoglycemia	5	2	10	0	17
%	29.41	11.76	58.82	0	100
Hypocalcemia	3	3	12	0	18
%	16.67	16.67	66.67	0	100
Hypernatremia	1	1	5	0	7
%	14.29	14.29	71.43	0	100
Cerebrovascular	1	0	2	0	3
%	33.33	0	66.67	0	100
Hypoxia	0	1	1	0	2
%	0	50	50	0	100
Meningitis	3	1	3	0	7
%	42.86	14.29	42.86	0	100
NN Hyperbilirubinemia	0	1	1	0	2
%	0	50	50	0	100
5th Day Seizure	0	1	0	0	1
%	0	100	0	0	100
Unknown	1	0	0	3	4
%	25	0	0	75	100

(Chi-square test=77.19, DF=27, P value=0.001, Association- Highly significant)

In our study as shown in above table, Birth Asphyxia which found to be the most common type of seizure in 49 neonates, subtle type of seizure in 26 (53.06%) neonates followed by tonic type in 16 (32.65%) cases and clonic type in remaining 6 (12.24%) cases. The 2nd most common cause of seizure in our series was metabolic abnormalities in 42 neonates in which subtle type was most common seizure type in 27 (64.28%) cases followed by 9 (21.42%) neonates having clonic type of seizure, 6 (14.28%) neonates had tonic type. Again, it was statistically highly significant showing association between a particular type of seizure and its etiology. Among all cases, 7 cases of seizures were due to meningitis, 3 (42.86%) cases had subtle seizure and clonic type and 1 case (14.29) clonic type. Out of the 2 cases of seizures due to hyperbilirubinemia one was subtle seizure and other one was of tonic type. Among seizures due to Cerebrovascular causes 2 (66.67%) were of subtle type and 1 (33.33%) cases of clonic type. Hypoxic seizure, 1 (50%) was of tonic type and 1 (50%) case was of subtle type. Among seizures due to unknown causes 3 (75%) were myoclonic type and 1(25%) was of clonic type.5th day seizure had 1 (100%) tonic type of seizure.

DISCUSSION

Neonatal seizures are aggressive signs and symptoms of neurological dysfunction in the newborn and usually presented as often muscular activity or autonomic changes.[7] neonatal Seizures are the most common neurological emergency which leads to high morbidity and mortality. The incidence of neonatal seizures was higher in very low birth weight infants (36.1 per 1000) as compared to birth weights of more than 2500 g (10.3 per 1000 in infants).[1] We conducted a single centre, prospective, non-interventional observational study of consecutive neonates admitted in neonatal intensive care unit. We observed and monitored 110 neonates with seizures admitted to NICU in our centre from December 2019 to November 2020. All subjects were evaluated on a clinical basis; physical examination was done to look for vitals, blood pressure, and cyanosis.

Demographic Profile:

During our study period of one year (December 2019 to November 2020), total of 3311 neonates were admitted in our neonatal intensive care unit of which 110 neonates had seizures. In our study, the incidence of neonatal seizures was 3.32%. As compared to this, the incidence of seizures in study carried out by Sheth R, Hobbs G, Mullett M [8] was 8.6%. The incidence of seizure in various studies carried out varied from 2.4% to 19.2% in following workers as 2.4% in study by Moayedi AR, Zakeri S, Moayedi F [9], 2.6% in Eghbalian F, Monsef A, Taghdiri MM [10] study and 19.2% in Digra SK, Gupta A [11] study.

The males' neonates outnumbered females, accounting for 61 (55.45%) cases, while females were 49 (44.55%) cases in our study which was similar with findings of the studies carried out by Moayedi AR, Zakeri S, Moayedi F [9,] in which 64 were male (58.2%) and 46 females (41.8%) and in study carried out by Eghbalian F, Monsef A, Taghdiri MM [10] 25/34 (73.55%) were males, 9/34 (26.5%) were females. A similar type of finding was also seen in study done by Digra SK, Gupta A [11], in which 72 out of 102 neonates were males and remaining 30 were females. The male to female ratio was 1.2:1 in our study. This preponderance of males over females in our study could be due to social beliefs (gender inequality). In our cross-sectional study full term neonates accounted for 86(78.18%) cases while preterm accounted for 22(20%) cases and post term accounted for 2(1.82%), which is consistent with other studies like Marzoki JMA [12], in which 84 out of 88 (95.4%) full term neonates had seizures.

In our study, 76 (69.09%) neonates have their birth weights more than 2.5 kg, while 32 (29.09%) neonates have birth weights in the range of 1.5 to 2.5 kg and 2 (1.82%) neonates have birth weight less than 1.5 kg. These findings from our study were similar with studies of Eghbalian F, Monsef A, Taghdiri MM [10], Digra SK, Gupta A [11], and Marzoki J M A [12], in which the most of the neonates had the birth weights more than 2.5 kg. Though our study consists of full term and pre term (108) neonates, few cases had complications like intra uterine growth retardation which is the reason they had birth weight in 1.5 to 2.5 kg group.

Type of Seizure

The most frequent seizure type found in our study was subtle seizure in 60 out of 110 neonates (54.55%), followed by tonic in 26 (23.64%) cases and clonic type in 20 (18.18%) cases. The similar findings as ours were seen in study carried out by Moayedi AR, Zakeri S, Moayedi F [9] which showed, the most common type of seizures observed was subtle (39.1%); the other types seen were myoclonic (17.3%), generalized tonic clonic seizures (GTCS) (12.7%), clonic 10%, tonic 7.3%, and in fifteen cases (13.6%) type of seizure was clubbed as others.

In another study carried out by Digra SK, Gupta A [11], majority 37.25% (38) neonates had generalized clonic seizures followed by other seizures like 26.47%, 23.52%, 12.74% subtle, tonic and focal clonic seizures respectively. In contrast to our study, most common seizure type was subtle in 28/88 (33.3%) neonates followed by tonic type of seizure in 18 (21.4%) neonates in a study done by Marzoki JMA[13].

Etiology of Seizure

In our study, the most common etiology of seizure was birth asphyxia (HIE) accounting for 49/110 (44.55%) cases. Metabolic abnormalities are 2nd most common cause accounting for 42/110 (38.18%) out of which hypocalcemia was the frequent cause in 18 (16.36%) out of 42 cases of metabolic causes followed by hypoglycemia in 17 (15.45%) cases and there was 7 (6.36%) case of hypernatremia. It was followed by meningitis in 7(6.36%) cases. There were 3 (2.72%) cases each of cerebrovascular cause. 2 (1.82%) cases of hypoxia and NN Hyperbilirubinemia. 4(3.64%) cases were of unknown cause. The study carried out by Moayedi AR, Zakeri S, Moayedi F [9] showed similar findings to our study, as HIE (36.4%) was common etiology of neonatal seizures, followed by infections (19.1%), metabolic disorders and inborn errors of metabolism (7.3%), Intra Cranial Hemorrhage (ICH) (2.7%) and structural disorders (1.8%); in thirty-six cases (32.7%) the etiology was not defined. In other study done by Eghbalian F, Monsef A, Taghdiri MM [10], the most common etiology of seizure was metabolic (followed by Birth asphyxia accounted for 2nd most common cause of seizure) which was somewhat different from our study findings, except hypocalcemia 9 (26.5%) was most common metabolic abnormality as in our study.

In another study done by Digra SK, Gupta A [11], showed birth asphyxia as the most common cause (67.65%) similar to our study followed by infections (septicemia& meningitis). In another study carried out by Marzoki JMA [13], metabolic cause was most common (47.7% cases) for neonatal seizures, followed by birth asphyxia in 15.4% cases.

But in this study hypomagnesaemia was most common metabolic abnormality observed instead of hypocalcemia in our study.

Relation of Etiology with Seizure Type

In our series we found that birth asphyxia (HIE) was the most repeated etiology of seizure amongst under which 26 (53.06%) cases were of subtle type, 16 (32.65%) cases were of tonic type, followed by 6 (12.24%) cases of clonic type. There was significant statistical association between seizure type and etiology. Seizures due to metabolic abnormalities had 42 (57.89%) cases were of subtle type 27(64.28%), 9 (21.42%) of clonic type and 6 (14.28%) of subtle type.

Hypoglycemic Convulsions

In our study hypoglycemia is the 2nd leading metabolic abnormality responsible for convulsion, 11 (68.75%) cases occurred in early neonatal period i.e., day 4 to 7, followed by 4(25%) cases between 2 to 3 day of life and 1(6.67%) on day 7 of life. The statistical association is significant such that hypoglycemic seizures occurred most commonly on day 4 to 7 of life. As compared to this in a study done by Marzoki JMA [13], majority of hypoglycemic convulsions (60%) occurred in first 2 days of life followed by 20% cases occurring in 3 to 7 days of life and after day 7 of life.

Hypocalcemia Convulsions

In our study hypocalcemia was the prime metabolic etiology, 10 (55.56%) cases occurred on day 2 to 3 of life followed by 5 (27.78%) cases on day 4 to 7 of life and 3 (16.67%) cases on day 1 of life. This finding was statistically significant. As compared to this in a study done by Marzoki JMA [9], 54.5% cases occurred in first two days of life followed by 36.4% cases occurring in day of life 3.

Outcome:

In our series of total 110 neonates enrolled at our centre, 6 neonates expired secondary to septicemia and complex congenital heart disease. 104 cases were discharged out of which many cases of birth asphyxia are still under regular follow up. Few cases had resistant seizures for which they are on levetiracetam.

CONCLUSIONS

Our incidence of neonatal seizures in hospitalized NICU was 3.32%. The gender ratio (male to female ratio) was 1.2:1 in current study. Birth asphyxia was the most common cause of neonatal seizures in our study, followed by metabolic abnormalities & meningitis. Birth asphyxia was the most common cause of seizures in preterm cases & the metabolic abnormalities (hypoglycemia, hypocalcemia and hypernatremia) in case term neonates.

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