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Original Research Article

Determination of the risk factors and underlying biochemical abnormalities of neonatal seizures in a tertiary care centre of South India

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ABSTRACT

Background: Neonatal seizures represent most common symptom rather than a cause for underlying functional brain abnormality. Commonly seen in first 48 hours of birth resulting in significant long-term morbidity and mortality causing impaired motor and cognitive functions in the childhood. Hence it become critically important for early diagnosis and treatment of neonatal seizures.
Methods: This prospective observational study took place in NICU of Al Ameen Medical college Vijayapura for period of 6 months including all neonates within 28 days of life presenting with seizures not on any anticonvulsants.
Results: Males were in majority with 58% with maximum onset within 24 hours of birth. Vaginal deliveries (66%), preterms (56%), SGA (62%) and LBW (54%) infants are high risk. Birth asphyxia and sepsis were identified to be most common underlying precipitating factors. Hypoglycaemia (38%) and hypocalcemia (28%) were the most common biochemical abnormalities found. Hypoglycaemia was more commonly found in preterm, LBW and SGA, whereas Hypocalcemia in term, LBW and AGA neonates. Hypoglycaemia was found to be significantly high with onset within 24 hours of birth. Sodium imbalance was the main cause identified in subtle seizures, hypoglycaemia in tonic seizures and Hypocalcemia in clonic type of seizures.
Conclusions: Quick assessment and timely diagnosis according to the etiology are necessary to prevent long term neurological outcome as it not only determines course of treatment but also associated morbidity and mortality. Biochemical abnormalities, if not treated properly, can result in poor prognosis therefore work up should be done in all neonates with seizures and should be included as routine investigation in all cases as they are easily treatable and can prevent long term morbidities.

Keywords: Biochemical abnormalities, Clonic seizures, Hypoglycaemia, Hypocalcaemia, Neonatal seizures, Risk factors, Subtle seizures, Tonic seizures

INTRODUCTION

Neonatal seizures are one of the most common causes of NICU admission with functional brain abnormalities, occurring in first 28 days of life. Commonly seen in first 48 hours of birth causing significant long-term morbidity and mortality causing impaired motor and cognitive functions in the childhood.[1,2] There are numerous factors responsible for neonatal seizures therefore it becomes rather challenging to identify etiology and accurate diagnosis in time. There is a significant impact of neonatal seizures on developing brain and their prognosis and mode of treatment depends on underlying etiology, however, in developing countries like us where continuous EEG monitoring is practically not available in most centers, clinical observation becomes the key for

diagnosis.[3] Therefore, our objectives of the study is to determine the clinical presentation and risk factors associated with neonatal seizures and to study the underlying biochemical abnormalities in association with neonatal seizures.

METHODS

This was a prospective observational study. This study was conducted in Neonatal ICU of department of Paediatrics in Al Ameen Medical College and Hospital, Vijayapur, Karnataka, India. The study duration was of 6 months from November 2023 to April 2024.

Sample size

The sample size taken was 50.

Inclusion criteria

All neonates from birth till 28 days presenting with seizures including both neonates who delivered at our institute and referred from outside where mothers/caretakers giving consent for the study.

Exclusion criteria

Babies already on anticonvulsant therapy. Mothers/ caretakers not giving consent for the study. All mothers/caretakers were explained about the study in details, including risks/ benefits, procedure, compliance etc. And voluntary informed written consent was taken from them.

Customized proforma

A customized proforma was designed specifically for the requirement of the study and all the information was collected on this proforma. Before giving any specific treatment, 2ml of blood was collected by sterile technique for following investigations like blood glucose, total serum calcium levels, serum sodium, serum potassium and serum magnesium levels.

Ethical approval

Ethical approval was taken from institute ethics committee.

Statistical analysis

Data was recorded on MS Excel sheets and analysis has been made. Descriptive analysis was carried out by mean and standard deviation for quantitative variables. Independent sample t test/ANOVA/ paired t test used to assess statistical significance. Number and proportion for categorical variables. Chi square test was used to test statistical significance. Data was also represented using appropriate diagrams like bar and pie diagrams. P value <0.05 was considered significant. Data analysis will be performed using SPSS software version 23 (IBM Statistics, Chicago, USA) and Microsoft Office 2007.

RESULTS

Out of 50 neonates, 33 (66%) were delivered vaginally, for 15 (30%) LSCS was done due to obstetric indications and for 2 (4%) of them, instrumental delivery was done using ventouse/forceps. It was seen that who were delivered vaginally have landed into seizures more as compared to those who were delivered by caesarean. When comparing gestational age among study group, 28 (56%) were preterm, 20 (40%) were term and 2 (4%) were post-term. Majority of neonates who suffered from seizures were preterm.

Table 1: Normal reference range for various biochemical indices in neonates.

Biochemical indices	Reference range
Serum sodium	135-145 mEq/l
Blood glucose	<40 mg/dl (capillary blood) <45 mg/dl (venous blood)
Total serum calcium	<7 mg/dl for preterm neonates <8 mg/dl for term neonates
Serum magnesium	1.5-2.5 mg/dl
Serum potassium	3.5-5.5 mg/dl

Comparison based on Classification of birth weight among neonates who suffered from seizures, 62% (n=31) were SGA, 34% (n=17) were AGA and 4% (n=2) were LGA. SGA had more chances of seizures as compared to others. 54% (n=27) neonates who suffered seizures had LBW followed by 30%(n=15) had NBW 12% (n=6) had VLBW and 4%(n=2) among them were Macrosomia. Lower birth weight has high propensity for neonatal seizures. 21 (42%) out of 50 neonates had seizures before 24 hours of birth, whereas 16 (32%) had seizures between 24-48 hours, 10 (20%) among them had seizures between 2-5 days and least of all, only 3 (6%) among them had seizures after 5 days. Majority had their onset of seizures before 24 hours of birth. Out of 50 neonates who suffered from seizures, birth asphyxia was seen in 15 (30%), 9 (18%) among them had sepsis, 8 (16%) was Infant of diabetic mothers. Other risk factors which were seen were PROM in 4 (8%) neonates, MSL in 5 (10%) and Preeclampsia in 5 (10%) also. Birth asphyxia and sepsis were the two factors which were common. Out of the total 50 neonates, 42 (84%) of them were delivered in the institute and 8 (16%) were referred from another institute.

Out of 50 neonates, we found biochemical abnormalities among 34 neonates. Incidence was 68%. 7 neonates were found to have combined hypoglycaemia and hypocalcaemia, whereas 3 among them had combined hypomagnesemia and hypocalcaemia.

Table 2: Distribution according to risk factors.

Variables	Frequency	%
Gender		
Males	29	**58**
Females	21	42
Mode of delivery		
NVD	33	66
Instrumental	02	4
LSCS	15	30
Gestational age		
Preterm	28	56
Term	20	40
Post-term	02	4
Classification of birth weight		
SGA	31	62
AGA	17	34
LGA	02	4
Birth weight		
VLBW	06	12
LBW	27	54
NBW	15	30
macrosomia	02	4
Age at onset (in hours)		
<24	21	42
24-48	16	32
48-120	10	20
>120	03	6
Predisposing factors		
IDM	08	16
Prom	04	8
Pe	05	10
Birth asphyxia	15	30
Sepsis	09	18
Msl	05	10
Place of delivery		
In born	42	84
Out born	08	16

Table 3: Analysis of biochemical abnormalities found in study population.

Biochemical abnormalities	Frequency	%
Hypoglycaemia	19	38
Hypocalcaemia	14	28
Hyponatremia	05	10
Hypomagnesemia	04	8
Hypernatremia	02	4

Among the study population, subtle seizures were the most common type found which was 56% (n=28) followed by tonic type of seizures i.e. 28% (n=14) followed by clonic seizures which were found to be only 16% (n=8).

Table 4: Correlation of gestational age and birth weight classification between neonates with seizures.

	Preterm (n=28)	Term (n=20)	Postterm (n=02)	Chi square value	P value
SGA	21 (75%)	10 (50%)	00	5.39	0.02/S
AGA	07 (25%)	09 (45%)	01 (50%)	6.11	0.04/S
LGA	00	01 (5%)	01 (50%)		

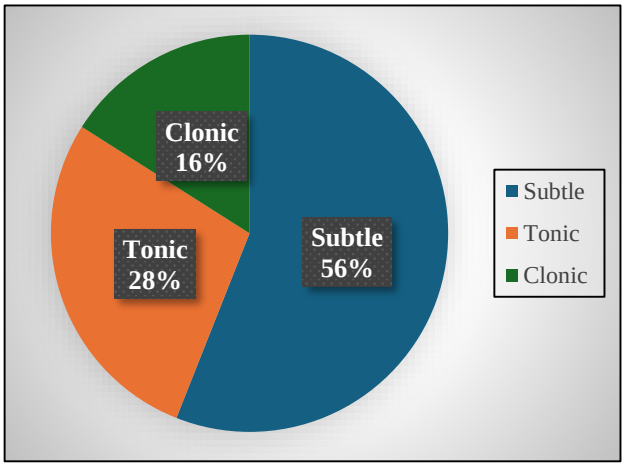

Figure 1: Classification of neonatal seizures among study population.

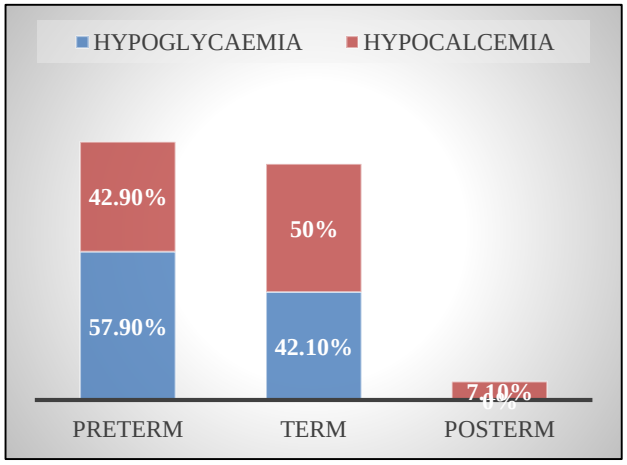

Figure 2: correlation of hypoglycaemia and hypocalcemia with gestational age of study population.

Upon analysing biochemical abnormalities among neonates with seizures, hypoglycaemia was the most common abnormality found i.e. 38%. Second most common abnormality was found to be hypocalcemia which is 28% followed by hyponatremia 10%, hypomagnesemia 8% and hypernatremia 4%. We found 21 preterm (SGA) with seizures significantly more common than preterm (AGA) and (LGA).

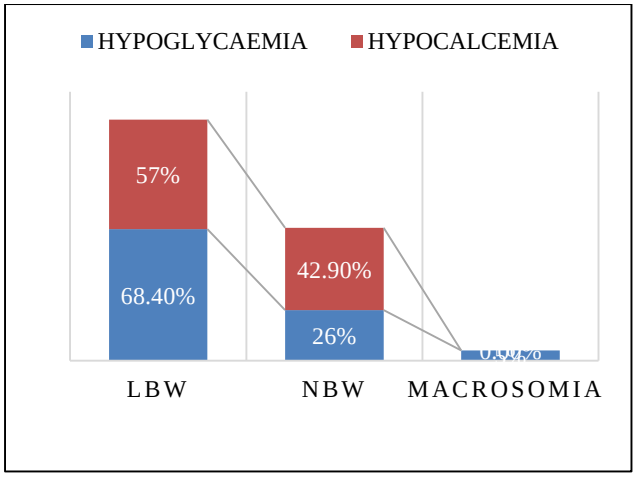

Figure 3: Correlation of hypoglycaemia and hypocalcemia with birth weight.

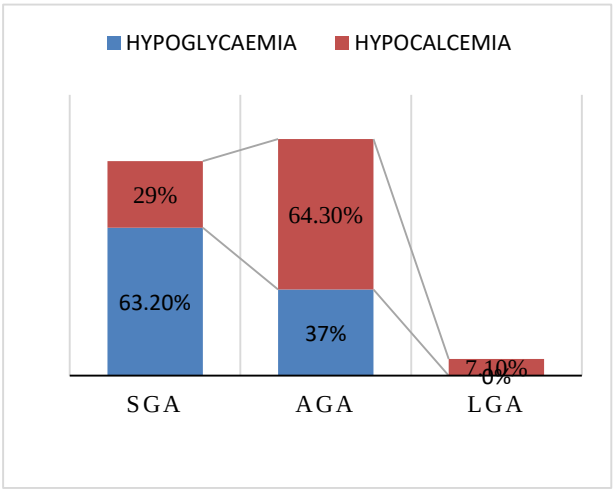

Figure 4: Correlation of hypoglycaemia and hypocalcemia with birth weight classification.

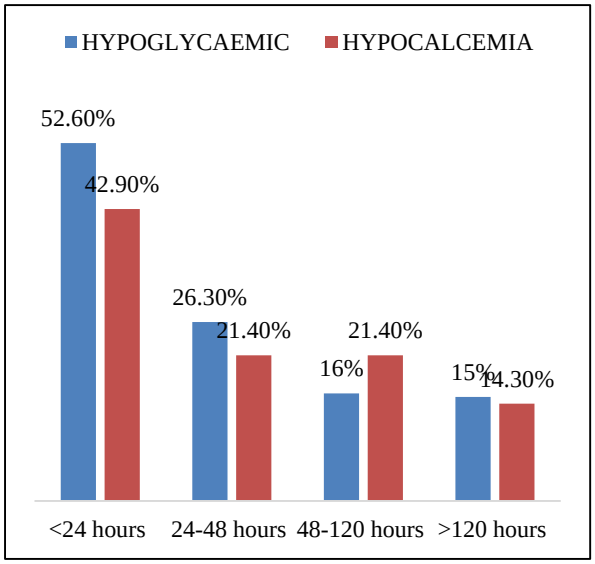

Figure 5: Correlation of hypoglycaemia and hypocalcemia with age at onset of seizures.

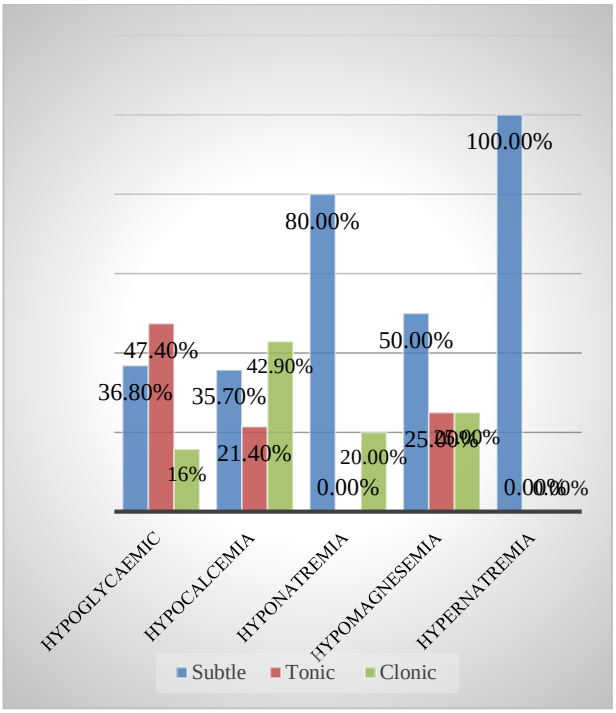

Figure 6. Correlation of biochemical indices with type of seizures

Term (AGA) is significantly more common than term SGA and LGA. Out of 19 cases of hypoglycaemia found, 11 (57.9%) were preterm while rest 8 (42.1%) were term. And for hypocalcemia in concern, term neonates were more 50% (n=7) as compared to preterm with hypocalcemia I.e. 42.9% (n=6) and postterm was 7.1% (n=1). In preterms, hypoglycaemia is more common (p=0.49, NS) whereas in terms, hypocalcemia was found to be more common (n=0.17, NS) but results are not significant.

When we compare birth weight, hypoglycaemia is more common in LBW I.e.in <2.5 kg neonates. 13 (68.4%) neonates out of 19 hypoglycaemic neonates had low birth weight (5;26.3% had VLBW and 8;42.1% has LBW) while only 5 (26.3%) had NBW and only 1 (5.3%) was macrosomic (p=0.15, NS).

Same with hypocalcemia which is found to be more common in LBW neonates I.e. 8 (57.1%) out of 14 had low birth weight (3;21.4% had VLBW and 5;35.7% had LBW) while the other 6 (42.9%) had normal birth weight (p=0.61, NS). Both hypoglycaemia and hypocalcemia were found to be more common in low-birth-weight neonates, but correlation is not significant. Hypoglycaemia is more common in SGA neonates 63.2% (n=12) than AGA neonates 36.8% (n=7) with seizures (p=0.25, NS). But the results were different for hypocalcemia, where we found that AGA neonates were more at risk for hypocalcemia (57.2%; 8) than SGA neonates (35.7%; 5) and LGA (7.1%; 01) (p=0.05, S). Prevalence of hypocalcemia was significantly more in AGA neonates than in SGA and LGA neonates. 52.6%

(n=10) neonates have Hypoglycaemia who had onset of seizures within 24 hours of life followed by 26.3% (n=5) had onset between 24-48 hours followed by 15.8% (n=3) had onset between 48 hours to 5 days followed by 5.3% (n=1) had onset of seizure after 5 days (p=0.02, S). Similarly, hypocalcaemia was found maximum in neonates who had their onset of seizure within 24 hours of life i.e., 42.9% (n=6) followed by 21.4% (n=3), 21.4% (n=3) and 14.3% (n=02) with onset at 24-48 hours, 48-120 hours and >120 hours respectively (p=0.46, NS).This shows that both hypoglycaemia and hypocalcemia is proportional to the onset of seizures, where hypoglycaemia is significantly found in neonates with seizure onset within 24 hours (p=0.02, S).

Biochemical indices are not exclusively found in any particular type of seizures. Some neonates have multiple biochemical abnormalities therefore results are not 100% comparable. In Subtle seizures, hypoglycaemia was found in 7 (36.8%) neonates while hypocalcaemia in 5 (35.7%), Hyponatremia in 4 (80%), Hypomagnesemia in 2 (50%) and Hypernatremia in 02 (100%) neonates. From our result it was found that sodium imbalance is the main cause for subtle type of seizure.

In tonic seizure, hypoglycaemia was found in 47.4% (n=09) while hypocalcaemia in 3 (21.4%) and hypomagnesemia in 01 (25%). Hypoglycaemia was found to be the probable cause for tonic type of seizures. In Clonic seizure, Hypocalcaemia was found in 42.9% (n=06), hypoglycaemia in 03 (15.8%), hyponatremia in 20% (n=01) and hypomagnesemia in 25% (n=01). Therefore, Hypocalcaemia was found to be main factor for clonic type of seizure.

DISCUSSION

Biochemical abnormalities, particularly hypoglycemia and Hypocalcemia, represents nearly half of the causes of neonatal seizures. These are present either as an underlying cause or due to an associated disease. And since, prognosis and the outcome of the neonates depends upon identifying the etiology of seizures, therefore from our study, we have tried to identify the underlying causes and associated biochemical abnormalities of neonatal seizures. In the present study, we have considered 50 neonates admitted in NICU of Al Ameen Medical College Vijayapura, Karnataka who presented with seizures, satisfying inclusion and exclusion criteria.

Gender distribution

In our study, out of 50 neonates, 58% were males and 42% were females. Overall M:F ratio was 1.38:1. In our study we found that males are more susceptible for seizures as compared to females. Study done by Aziz et al[4] (60% males) and Dinesh Das et al[5] (62.6% males), both reported male predominance. In another study done by Tekgul et al showed male:female ratio to be 1.15:1 whereas Sudia et al reported 1.73:1further supporting my study that seizures are common in males.[6,7]

Gestational age

56% of preterm were found to be affected in our study as compared to term and post-term neonates. Also, when compared birth weight classification SGA (62%) neonates have more risk for seizures than AGA (34%) and LGA (4%) neonates. This result is similar to the study done by Ronen and Gabriel et al[8] where they found preterm neonates are 6 times more prone for neonatal seizures as compared to term neonates. Similar results were found in study of Scher and Aso et al, where they found incidence of seizures was higher in preterm infants.[19]

Birth weight

In our study we found that low birth weight neonates (52%) are more likely to have seizures as compared to normal birth weight neonates (40%). The findings of Kohlet et al is corroborate with the present study.[10]

Mode of delivery

In my study, 66% neonates born by normal vaginal delivery, 30% by caesarian section and 4% by forceps delivery. Aziz et al, in his study also reported similar incidence of neonatal seizures were higher in those born by normal vaginal delivery (48%) followed by caesarian section (28%) and least in operated vaginal (24%).[4]

Age at onset

From our study, we conclude that Maximum seizures occur within first 3 days of birth as 74% of the seizures are within 3 days. The results of Dinesh Das et al where they reported 71.3% seizures and Nawab et al reported 73.6 %seizures occur within 3 days which were comparable with my study.[5,11]

Predisposing factors

When we study the predisposing maternal and neonatal factors for seizures, we found that birth asphyxia (30%) and sepsis (18%) are the 2 most common factors identified. Results are corroborative with the study of Anand et al where they concluded HIE and sepsis contributed the commonest etiologies for neonatal seizures and Rennie et al, where he found birth asphyxia to be the commonest cause of seizures.[12,13]

Classification of seizures

In our study, most common seizure found was subtle seizure with the incidence of 56% followed by 28% neonates with tonic seizure and least was clonic seizure in 16%. Similar findings were reported by Sudia et al[7] where subtle seizures occurred in 63.33% followed by

generalized tonic in 19.33% and multifocal clonic in 10% of neonates. Similarly subtle seizures were found to be most common in studies done by Dinesh das et al, and Park Weon et al, which were corroborated with my study.[5,14]

Biochemical abnormalities

In our study 34 babies out of 50 (68%) have found to have some biochemical abnormalities. Comparable result was found in study by Kumar et al[15] where he observed biochemical abnormalities in 62.8% of neonates. Hypoglycaemia (38%) and hypocalcemia (28%) were the most common biochemical abnormalities found in our study. Suganthi et al, reported similar observations that hypoglycemia (43.8%) and hypocalcemia (35.4%) were the most common biochemical abnormality found in neonatal seizures. Jain et al, shah et al and Prasad et al also found similar results further supporting my study.[16-19]

Only clinical criteria taken to identify neonatal seizures because of unavailability of continuous video EEG, so might have missed electro graphic seizures. Over diagnosis or under diagnosis based on inter observer variation and lack of continuous in function cerebral monitor. Shorter duration and small sample size.

CONCLUSION

Identifying underlying risk factor for the onset of neonatal seizures are bit challenging and quite necessary as it determines the course of action and neonatal outcome. From our study, we have determined biochemical abnormalities as the major prognostic determinant. Therefore, we recommend to do biochemical work up in all neonates with seizures and should be included as first line investigations.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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