JMCH Journal of Maternal and Child Health (2022), 07(02): 222-230
Masters Program in Public Health, Universitas Sebelas Maret

Research

A Comparative Study of the Incidence of Hypoglycaemia and Hypocalcaemia in Neonatal Seizures Occurring within 72 Hours of Birth Admitted in NICU at a Tertiary Care Centre

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ABSTRACT

Background: Recognition of hypoglycaemia and hypocalcaemia in Neonatal seizures is important for to prompt diagnosis and therapeutic implications. Study aimed to analyse the incidence of hypoglycaemia and hypocalcaemia in neonatal seizures occurring within 72 hours of birth in 32-37 weeks preterm and term (37-42 weeks) babies.
Subjects and Method: A prospective hospital based observational study enrolled total of 105 neonates presenting with seizures activity within 72 hours of birth admitted to NICU of SV Medical College, Tirupati from September 2013 to October 2014. Samples selected by Simple random sampling method. Detailed antenatal, natal and postnatal history including CNS examination were taken and investigations estimated includes complete blood counts and picture, random blood sugar, and serum ionic calcium. The analysis data was chi square test with SPSS for Windows (Ver 20), SPSS Inc. New York.
Results: The results was In neonatal seizures occurring within 72 hours of birth, hypoglycaemia (62.9%) was common, more so in preterm babies both hypoglycaemia 9 (37.5%) and combination of hypoglycaemia and hypocalcaemia 9 (37.5%). The association between type of delivery and hypoglycaemia/ hypocalcaemia shown significant different (p=0.002). The association between Birth Weight and hypoglycaemia/ hypocalcaemia shown a very high significant different (p< 0.001).
Conclusion: In neonatal seizures occurring within 72 hours of birth, hypoglycaemia (62.9%) was common, more so in preterm babies both hypoglycaemia 09 (37.5%) and combination of hypoglycaemia and hypocalcaemia 09 (37.5%).

Keywords: neonatal seizures, hypoglycaemia, hypocalcaemia.

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Cite this as:
Rahman ZU, Khaleef SA, Basha SMS, Krishnaiah DM (2022). A Comparative Study of the Incidence of Hypoglycaemia and Hypocalcaemia in Neonatal Seizures Occurring within 72 Hours of Birth Admitted in NICU at a Tertiary Care Centre. J Matern Child Health. 07(02): 222-230. https://doi.org/10.26911/thejmch.-2022.07.02.11.

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BACKGROUND

Neonatal seizure is a common neurological problem in the neonatal period with a frequency of 1.5 to 14/1000 neonates (Reddy et al., 2018). Neonatal seizures have always been a topic of particular interest because of their universal occurrence (Das et al., 2016). A varied number of conditions are capable of causing seizures in the neonatal period. Seizures are the most distinctive manifestation of significant CNS disease in the new-born, prompt diagnosis and intervention are indicated because not only do seizures often indicate serious under-

lying disease, but they may also interfere with supportive care example, ventilation and alimentation (Reddy et al., 2018). Repeated seizures are often with hypoventilation and apnoea which, in turn, may result in cardiovascular collapse and ischaemic brain injury.

Furthermore, the hypercapnia in combination with increased lactate and an adaptive rise in systemic BP, may result in an abrupt rise in cerebral blood flow with associated risk of intracranial hemorrhage especially in premature infants, also neonatal seizures have deleterious effect on the developing brain by depleting cerebral glucose levels, which in turn may interfere with DNA synthesis, glial proliferation, differentiation and myelination as suggested by experimental animal studies (McLean et al., 2012). Neonatal seizures differ considerably from seizures observed in older children, principally because the immature brain is less capable of propagating generalized or organized electrical discharges (Mizrahi et al., 2005).

Since neonatal seizures have an adverse effect on neurodevelopment and can predispose to cognitive and behavioural epileptic complications later in life, prompt diagnostic and therapeutic plans are necessary. Determining the underlying etiology for neonatal seizures is critical. In the new-born seizures are always due to an underlying cerebral or biochemical abnormality (Shah et al., 2008). Among metabolic causes hypocalcaemia, hypomagnesemia, hypoglycaemia and hyponatremia account for less than 10% of cases of neonatal seizures but remain important because they are readily treatable (Vasudevan et al., 2013; Connell et al., 1989).

Aim of this study is to analyse the incidence of hypoglycaemia and hypocalcaemia in neonatal seizures occurring within 72 hours of birth in 32-37 weeks preterm and term 37 – 42 weeks babies.

SUBJECTS AND METHOD

1. Study Design

A prospective hospital based observational study enrolled total of 105 neonates presenting with seizures activity within 72 hours of birth admitted to NICU of SV Medical College, Tirupati from September 2013 to October 2014.

2. Population and Sample

Neonates with seizure activity within 72 hours of birth in term (>37 weeks) and 32-37 weeks premature newborns at NICU were included in the study.

Neonates with birth asphyxia, or with intraventricular haemorrhage, or with sepsis History of meconium aspiration/ meconiumstained amniotic fluid, and Neonates with Congenital anomalies were excluded from the study.

Sample size was calculated based on the following formula, on the basis of the previous study (Manoj et al., 2019). The precision was 5% and the confidence interval was 95% for estimating single proportion is given by:

$$n = [Z2\ 1\text{-}\alpha/2 \times p \times (1\text{-}p)]/d2 = [(1.96)2$$

So, sample size was 105 subjects. Sample technique was simple random sampling technique.

3. Study Variables

Independent and dependent variables related to neonatal seizures were recorded.

Antenatal history: age and parity of mother were noted. History of whether regular ANC checkups were done or not was enquired history of medical illness like diabetes, fever during pregnancy were asked. History of obstetric complications like PIH, eclampsia, antepartum hemorrhage, oligo or polyhydramnios were taken and history regarding medication enquired.

Perinatal history: history of PROM, prolonged second stage of labour, meco-

nium staining of liquor, place of delivery, type of delivery and indication for forceps and caesarean section were enquired. After delivery whether baby cried immediately or not, was it meconium stained and any resuscitation done, were enquired. If APGAR score was done, it was noted, and medication given to the baby were recorded.

Postnatal history: history of lethargy poor feeding, jaundice, excessive cry, fever, vomiting and seizures were taken.

History of seizures: clinical details of each seizure episode reported by the mother and subsequently observed by resident doctors on duty were recorded, i.e., age of onset of seizures, type of seizures, the duration of seizures, number of seizures and consciousness during and between seizures were taken. The neonatal seizures were classified according to Volpe's classification into multifocal, clonic, focal tonic, tonic and myoclonic. After appropriate history, detailed examination of neonate was done.

Examination: basic anthropometry of the neonate was recorded, and gestational age was assessed according to New Ballard Scoring. Vitals of neonates (HR, RR, peripheral pulses, blood pressure, temperature, capillary filling time); General physical examination of neonate to know disparity in head size and shape, skin lesions were noted. CNS examination was done as per the proforma. Other systems were also examined. Complete blood counts: Sepsis screening, which include Peripheral smear for band cells and toxic granules, CRP and blood culture if necessary.

4. Operational Definition of Variables

As per study by Kumar et al. (2005):

Hypoglycemia: blood sugar <45 mg/dL (normal range: 45 - 150 mg/dL).

Hypocalcaemia was defined when total serum calcium: Term newborn/premature >1.5 kg - <1.1 mmol/L (4.4 mg/dl); Premature <1.5 kg-- < 1 mmol/L (4 mg/dl).

5. Study Instruments

Random blood sugar was done urgently with glucostick and then confirmed by Glucose Oxidase Peroxidase method by Beckman coulter AU480 chemistry analyser, Roche. Serum calcium was estimated photometrically by using the semi autoanalyzer by O-cresolphthalein complexone method (Connerty et al., 1966).

6. Data analysis

Data was collected in accordance with the proforma. Continuous variables such as demographics and laboratory parameters are presented as mean ± standard deviation. Numbers and percentages were used to express categorical variables. The unpaired t test was used to assess differences in quantitative variables between groups. The chi square test was used to analyze categorical variables, while multivariate analysis was used to evaluate dependent variables and the t test was used to evaluate continuous variables. In all statistical tests, a p value of less than 0.05 was used to indicate a significant difference. All the statistical operations were done through SPSS for Windows (V20), SPSS Inc. New York.

7. Research Ethics

The research related to human use complies with all the relevant national regulations, institutional policies, is in accordance with the tenets of the Helsinki Declaration, and has been approved by Institutional Ethics Committee, SV Medical College, Tirupati-517507, India (dated 25/08/2013). Informed consent obtained from parents/guardian of all neonates.

RESULTS

Out of 105 neonates studied, 81 were full term, of which 69 (65.4%) were AGA and 12 (11.4%) SGA, 24 (22.9%) were preterm. Neonate seizure activity within 72 hours of birth more commonly in term-AGA babies (65.7%).

Number of males were 63 (60%), and in females were 42 (40%). In preterm, male numbered 15, and female numbered 9. In term, males numbered 48, and female numbered 33. Neonate seizure activity within 72 hours of birth more commonly in male babies with male to female ratio1.5:1. Most of the neonatal seizures occurring within 72 hours of birth in hospital deliveries in 90 (85.7%) cases. Most of them were delivered by normal vaginal delivery in 66(60%) cases. Caesarean deliveries were 36 (37.1%). Total number of cases of preterm delivered at home were 03 and at hospital were 21.

Table 1 shows total number of cases term by normal vaginal delivery were 57 and by caesarean section were 21. Preterm delivered by normal vaginal delivery were 9 and by caesarean section were 15.

54.3% neonatal seizures occurring within 72 hours of birth in new-borns weighing >2.5 kg. Birth weight in between 1.5 kg to 2.5 kg were 33 (31.4%), 1 kg to 1.5 kg were 09 (8.6%) and less than 1 kg were 06 (5.7%). Most neonatal seizures occur in the 24 hours of life, i.e., 48.5%. the highest number is seen on first day of life (57.4%). Subtle seizures are the commonest type of seizures (42.9%) followed by generalized tonic (28.5%), clonic (14.3%), and mixed type of seizures (14.3%).

Table 1. Distribution of neonates according to type of neonatal seizure, Birth weight, and Time of onset of seizures

Variabel	Variable	Number of neonates, n (%)
Birth weight (Kg)	> 2.5	57 (54.3%)
	1.5 – 2.5	33 (31.4%)
	1 – 1.5	9 (8.6%)
	< 1	6 (5.7%)
Type of seizure	Subtle	45 (42.9%)
	Generalized tonic	30 (28.5%)
	Clonic	15 (14.3%)
	Mixed	15 (14.3%)
Time of onset of neonatal seizures (in hours)	< 6	18 (17.1%)
	6 – 24	33 (31.4%)
	24 – 36	27 (25.7%)
	36 – 48	24 (22.9%)
	48 – 60	3 (2.9%)
	60 – 72	00

Table 2 shows incidence of hypoglycaemia in neonatal seizures common in Term-AGA 51 (77.3%), hypocalcaemia also more common in Term-SGA 09 (50%) and both hypoglycaemia and hypocalcaemia common in Term-AGA (75%) and in preterm 9 (10.7%).

Incidence of hypoglycaemia high in male 42 (63.3%) than female, hypocalcaemia is equally distributed in both gender and incidence of both hypoglycaemia and hypocalcaemia was high in male 12(57.1%). The difference was statistically non-significant.

Incidence of hypoglycaemia high in institutional deliveries 57 (86.4%) than home deliveries, hypocalcemia is high in institutional deliveries 15(83.3%) and incidence of both hypoglycemia and hypocalcemia was high in institutional deliveries 18 (85.7%).

Incidence of hypoglycaemia high in normal vaginal deliveries 48 (72.7%) than other type of deliveries, hypocalcaemia is equally distributed in both normal vaginal and caesarean deliveries and incidence of

both hypoglycaemia and hypocalcaemia was high in caesarean deliveries 15 (71.4%). The difference is statistically significant.

Incidence of hypoglycaemia high in birth weight greater than 2.5 kg 45 (68.2%), hypocalcaemia is most common in birth weight 1.5 to 2.5 kg 12 (66.7%) and incidence of both hypoglycaemia and hypocalcaemia was high in birth weight 1 kg to 1.5 kg 09 (42.8%).

Table 2. Distribution of neonates according to gestational age, gender, place/type of delivery, baby birthweight and biochemical abnormality

	Hypoglycaemia (n=66)	Hypocalcaemia (n=18)	Hypoglycaemia & Hypocalcaemia (n=21)	P
Gestational age				
Term – AGA (n=69)	51 (77.3%)	9 (50%)	9 (75%)	0.020
Term – SGA (n=12)	6 (9.1%)	3 (16.7%)	3 (14.3%)	
Preterm (n=24)	9 (13.6)	6 (33.3%)	9 (10.7%)	
Gender				
Male	42 (63.3%)	9 (50%)	12 (57.1%)	0.550
Female	24 (36.4%)	9 (50%)	9 (42.9)	
Place of delivery				
Institutional	57 (86.4%)	15(83.3%)	18 (85.7%)	0.900
HOME	9(13.6%)	3(16.7%)	3 (14.3)	
Type of Delivery				
Normal vaginal	48 (72.7%)	9 (50%)	6 (28.6%)	0.002
Caesarean	15 (22.7%)	9 (50%)	15(71.4%)	
Outlet forceps	3 (4.6%)	0	0	
Birth Weight (Kg)				
>2.5	45 (68.2%)	6 (33.3%)	6 (28.6%)	< 0.001
1.5-2.5	18 (27.3%)	12 (66.7%)	3 (14.3%)	
1-1.5	0	00	9 (42.8%)	
< 1	3(4.5%)	00	3 (14.3%)	

Table 3 shows incidence of hypoglycaemia high in seizures occurring within 6 hours of birth 24 (36.4.%), hypocalcaemia was high within 36-48 hours 15 (83.3%) and incidence of both hypoglycaemia and hypocalcaemia was high within 6 hours onset of seizures.

In hypoglycaemic seizures most common type of seizures were subtle 30 (45.5%), in hypocalcaemia seizures, common type of seizures was subtle type 09 (49.9%) and in both hypoglycaemia and hypocalcaemia seizures were least type was mixed type 03 (14.2%).

Table 4 shows that there are 4 comparative studies related to hypocalcemia and prevalence of hypoglycemia.

Table 3. Distribution of neonates according to type of seizures, time of onset of seizure and biochemical abnormality

Variabel	Hypoglycaemia (n=66)	Hypocalcaemia (n=18)	Hypoglycaemia & Hypocalcaemia (n= 21)	P
Type of seizure				
Subtle	30 (45.5%)	9 (49.9%)	6 (28.6%)	0.330
Generalized tonic	21 (31.8%)	3 (16.7%)	6 (28.6%)	
Focal	6 (9.1%)	3 (16.7%)	6 (28.6%)	
Mixed	9 (13.6%)	3 (16.7%)	3 (14.2%)	
Time of onset of seizure in hours				
<6 hrs	9 (13.6%)	0	9 (42.8%)	0.110
6-24 hrs	24 (36.4%)	3 (16.7%)	6 (28.6%)	
24-36 hrs	21 (31.8)	0	6 (28.6%)	
36-48 hrs	9 (13.6%)	15 (83.3%)	0	
48- 60 hrs	3 (4.6%)	0	0	
60-72 hrs	0	0	0	

Table 4. Comparative studies related to hypocalcemia and hypoglycaemia prevalence

Studies	Hypocalcaemia		Hypoglycaemia		Both hypoglycaemia & hypocalcaemia		Total	
	N	%	N	%	N	%	N	%
Present study	6	17.1	22	62.9	7	20	35	100
Sood et al. (2003)	7	70	4	40	-		10	100
Ronen et al. (1999)	-	-	3	17.6	-		17	100
Kumar et al. (2007)	9	42.8	10	47.6	-		21	100
Tekgul et al. (2006)	-	-	2	66.6	-		3	100

DISCUSSION

In the present study, majority of the neonates with seizure were full term babies, which is similar in a study by Moayedi et al (2007).

In a study by Lakra et al. (2003), majority of the neonates were born by normal vaginal delivery, followed by LSCS and forceps delivery. Our study results are in line with the above study findings, where majority were normal delivery accounts 60%, followed by caesarean deliveries, and forceps delivery.

In our study, majority were hospital deliveries, and next to home deliveries. Similarly, study by Moayedi et al. (2007) showed 73.6% of neonates were of >2.5 kg and 22.7% were <2.5 kg. These results were similar to our study

In the present study, the onset of seizures occurred within 24 hours in 48.5% of neonates. While in a study by Kumar et al. (2007), 75% of seizure episodes occurred before 115 hours of age, 57.8% developed seizure within first 48 hours of life. Onset of seizures within first 3 days constitutes the majority of cases, more so within first 48 hours of life.

In our study, the common type of seizure activity was Subtle in 42.9% neonates, followed by generalized tonic type. Similarly, study by Kumar et al. (2007) shows 46.55% were subtle seizures, and 21.55% were generalised tonic seizures. While Brunquell (2002) study shows subtle seizures in 51%, followed by focal clonic, and multifocal clonic and GTS.

In contrary to older children and adults, neonates present with subtle and generalised tonic seizures more commonly

because of immaturity of central nervous system and more mature limbic system compared to other parts of CNS in neonates. Subtle seizures are difficult to recognize and also difficult to interpret, as they may be normal neonatal activity and one should be careful in assigning subtle movements as seizures in neonates.

In our study, the incidence of hypoglycaemia high in seizures occurring within 6 hours of birth, which accounts 36.4%, while hypocalcaemia was high within 36-48 hours, which accounts 83.3% and the incidence of both hypoglycaemia + hypocalcaemia was high within 6 hours onset of seizures.

In our study, the incidence of hypoglycemia and incidence of hypocalcaemia in neonatal seizures common in Term-AGA, and similarly both hypoglycemia + hypocalcemia incidence was common in Term-AGA than in preterm with statistically significant difference.

The incidence of hypoglycemia was high in male neonates than female, while hypocalcemia is equally distributed in both gender and the incidence of both hypoglycemia+hypocalcemia was high in male than female with statistically significant difference.

In our study, the incidence of hypoglycemia and the incidence of hypocalcemia were high in hospital deliveries than home deliveries, while the combined incidence of both hypoglycemia+hypocalcemia were high in hospital deliveries.

Incidence of hypoglycemia high in normal vaginal deliveries 48 (72.7%) than other type of deliveries, hypocalcemia is equally distributed in both normal vaginal and caesarian deliveries and incidence of both hypoglycemia and hypocalcemia was high in caesarian deliveries 15 (71.4%) which is statistically significant.

The incidence of hypoglycemia is high in birth weight > 2.5 kg, which accounts 68.2%, while the incidence of hypocalcemia is common in birth weight between 1.5 to 2.5 kg 12, which accounts 66.7% and the incidence of both hypoglycemia + hypocalcemia was high in birth weight between 1 kg to 1.5 kg 09 (42.8%).

In a study of hypoglycaemia by Lilien et al. (1980), 41% of hypoglycemic neonates were SGA babies. Whereas in a study by Singhal et al. (1992) showed, of 2,248 babies preterm babies had three times increased risk (12.8%) as compared to term babies (3.6%) for hypoglycaemia and that (30.2%) manifest as seizures.

In neonatal seizures occurring within 72 hours of birth, hypoglycaemic seizure was common, and also high in preterm babies, the combination of hypoglycaemia and hypocalcaemia were commmon. Hence the recognition of hypoglycemia and hypocalcemia in neonatal convulsions is crucial and prompt treatment of respective metabolic abnormality is important to avoid landing into sequale .

AUTHORS CONTRIBUTIONS

Design: Zia Ur Rahman; Literature: Zia Ur Rahman; Data acquisition: Zia Ur Rahman; Statistics analysis: Sajid Basha, Murali Krishnaiah; Manuscript preparation: Zia Ur Rahman, Abdul Khaleef, Sajid Basha; Critical review and Approved: Zia Ur Rahman, Abdul Khaleef, Sajid Basha, Murali Krishnaiah.

FUNDING AND SPONSORSHIP

This work does not receive grant from funding agencies/ commercial sectors.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest in this study.

ACKNOWLEDGMENT

We acknowledge Kireeti for supervision, and other staff of SV Medical College and S.V.R.R. Govt general Hospital, Tirupati for their co-ordination during the study.

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