ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

Association of neonatal seizures and metabolic abnormalities in a rural tertiary hospital.

Dr. Jayashree P Jadhav[1], Dr. Gannu Sneha[2]*, Dr. Bhushan Deo[3], Dr. Kevin Sanjay Shah[4]

1. Head of the Department, Department of Pediatrics, Dr. Vitthalrao Vikhe Patil Pravara Rural Hospital, Loni, Maharashtra, India, Email- jpj.sangamner@gmail.com
2. Post graduate student, Department of Pediatrics, Dr. Vitthalrao Vikhe Patil Pravara Rural Hospital, Loni, Maharashtra, India, Email- sneha.jawaharlal@gmail.com
3. Professor, Department of Pediatrics, Dr. Vittalrao Vikhe Patil Pravara Rural Hospital, Loni, Maharastra, India. Email- bhushandeo40@gmail.com
4. Post graduate student, Department of Pediatrics, Dr. Vitthalrao Vikhe Patil Pravara Rural Hospital, Loni, Maharashtra, India, Email- kevinshah940@gmail.com

ABSTRACT

Background: Neonatal seizures are the episodes of abnormal electrical activity in the newborn brain typically within first 28 days of life. The study is based on the metabolic abnormalities associated with seizures. The presence of neonatal seizures has been found to be associated with poor neurodevelopmental outcome. If no prompt recognition or treatment. **Aim:** To study the clinic investigative spectrum of neonatal seizures associated with metabolic abnormalities. **Objectives:** To study the clinical presentation of seizures in neonate. To study the biochemical profile with seizure in neonate. **Design:** Observational cross sectional study. **Study period:** 2 years from June 2022 – June 2024. **Settings:** Department of pediatrics at Dr Balasaheb Vikhe Patil, Rural Medical College, Loni. **Methodology:** In all the neonates enrolled in the study, details of history, examination and investigation and treatment given were recorded in the predesigned proforma. Descriptive statistical analysis was done using SPSS 16 software. **Results:** Out of 106 neonates admitted in neonatal intensive care unit with neonatal seizures. Of these 59.4% were males and 40.5% were females. Normal birth weight babies were 45.2%, low birth weight were 49% and very low birth weight babies 5.6%. Out of 106 neonatal seizures 38 neonates have seizures due to metabolic abnormalities. Amongst the metabolic disturbances 57.8% had hypoglycemia, 23.6% had hypocalcaemia, 5.26% had hypomagnesaemia, 13.15% had hyponatremia. Most common seizures in metabolic disturbances were clonic type followed by tonic type followed by subtle seizures.

Keywords: Neonatal seizures, metabolic abnormalities, rural tertiary hospital

INTRODUCTION:

Metabolic disorders:

Hypoglycemia:

Hypoglycemia is the most common metabolic problem in neonates in the new born nursery and neonatal intensive care unit and is a trigger of neonatal seizures.

Many studies have shown that neonatal hypoglycemia may results in hypoglycemic neurological injuries, i.e., neonatal hypoglycemic brain injuries

According to **AMERICAN ACADEMY OF PEDIATRICS**,

Symptomatic infants i.e., late preterms, term small and large for gestational age babies i.e., both SGA and IGA , Infant of diabetic mothers - Hypoglycemia is defined as <40mg/dl

And in neonates <4 hours: <40mg/dl; 4-24 hours: <45mg/dl

Hypoglycemia in neonates can be associated with brain damage such as seizures, developmental delay, or long-term neuronal loss, and frequently occurs in neonatal infants with birth asphyxia, diabetic mothers, or low birth weight for gestational age.

Differential diagnosis of hypoglycemia:

Hypoglycemia is classified as transitional and persistent hypoglycemia

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

TRANSITIONAL / NON PATHOLOGIC HYPOGLYCEMIA: usually lasts for 24 hours can extend up to 72 hours, In utero the baby will have continuous supply of the glucose after sudden cut of umbilical cord there is sudden drop in the glucose levels and regulation is difficult for the newborn normal healthy individuals will get back to normal within 3-4 hours but the high risk and SGA babies will have difficulty to regulate to normal .

Neonates with this condition will have low levels of FFAs and less muscle stores of amino acids and no production ketones adequately and hyper insulinemia due to the B cell immaturity in regulation and also expression and will have inadequate hepatic glycogen stores.

Sometimes it can lasts for many days:

Early Transitional Adaptive Hypoglycemia: (adaption, IDM, infants of hypothermia, asphyxiated infants).

Secondary Associated Hypoglycemia: (Illness, sepsis, perinatal asphyxia, intracranial hemorrhage)

Persistant Hypoglycemia / Refractory Hypoglycemia:

Hypoglycemia lasts for >72 hours, normally transitional hypoglycemia can also last for 6 months sometimes but this persistent hypoglycemia is more prolonged and more severe and can be associated with some pathological conditions like congenital hyperinsulinemia, endocrine disorders, inborn errors of metabolism.

Persistent hypoglycemia is also more likely associated with possible neurologic sequel Congenital hyperinsulinism: (older names nesidioblastosis, idiopathic hypoglycemia, persistent hyperinsulinemia) Inappropriate excessive production of insulin from beta cells of pancreas

Initial management: Dextrose 10%, 2–3 mL/kg IV.

Hypocalcemia:

Neonatal hypocalcaemia, determined by either total serum calcium <8 mg/dL (2 mmol/L) or ionized calcium <4.4 mg/dL (1.1 mmol/L) for term infants.

This levels can little vary according to the gestational age and day of life

Hypocalcaemia is most common disorder seen both in terms and preterms, Late onset hypocalcaemia is more common in infants of developing countries because of the high phosphate containing formula feed or cow milk.

Risk factors:

1. Infant of Diabetic Mother
2. Perinatal stress
3. Intra uterine growth retardation
4. Nutritional deprivation
5. Hypomagnesaemia
6. Congenital abnormalities: (Digeorge Syndrome)
7. Maternal hyperparathyroidism

Initial treatment:

Hypocalcaemia Calcium gluconate, 5% (50 mg/mL) 100–200 mg/kg IV; 10% (100 mg/mL) 50–100 mg/kg IV if inadequate time for dilution

Hypomagnesemia:

It is a type of metabolic disorder which is very rare cause of neonatal seizure, it is mostly seen in preterm neonates and almost always associated with hypocalcaemia, there are 2 types of hypomagnesaemia.

- PRIMARY HYPOMAGNESEMIA: it is a very rare cause, and it is mostly due to defect in absorption or handling of magnesium
- INHERITED HYPOMAGNESEMIA: this type includes diseases such as severe primary hyperparathyroidism, hypomagnesaemia with secondary hypocalcaemia.

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

Hyponatremia and Hypernatremia:

Both the sodium causes i.e., hyponatremia and hypernatremia are uncommon causes of neonatal seizures. This occurs mainly due to improper fluid management and in neonates hyponatremia can be the result of Syndrome of inappropriate anti diuretic harmone (SIADH). In the setting of asphyxia, infection and trauma.

MATERIALS AND METHODS:

This study was carried out in the neonatal intensive care unit of Dr. BVP hospital, Loni. Attached to the pediatric department of PMT Rural medical college, Loni, Maharashtra. The study included the clinical profile of 106 neonates with neonatal seizures during the period of June 2022-June 2024 after approval from the ethical committee.

Our study is an observational cross sectional study..

Inclusion criteria:

- Neonates (< 28 days of life) clinically diagnosed with seizures.

Exclusion criteria:

- Neonates (<28 days of life), with no parental consent for the study.

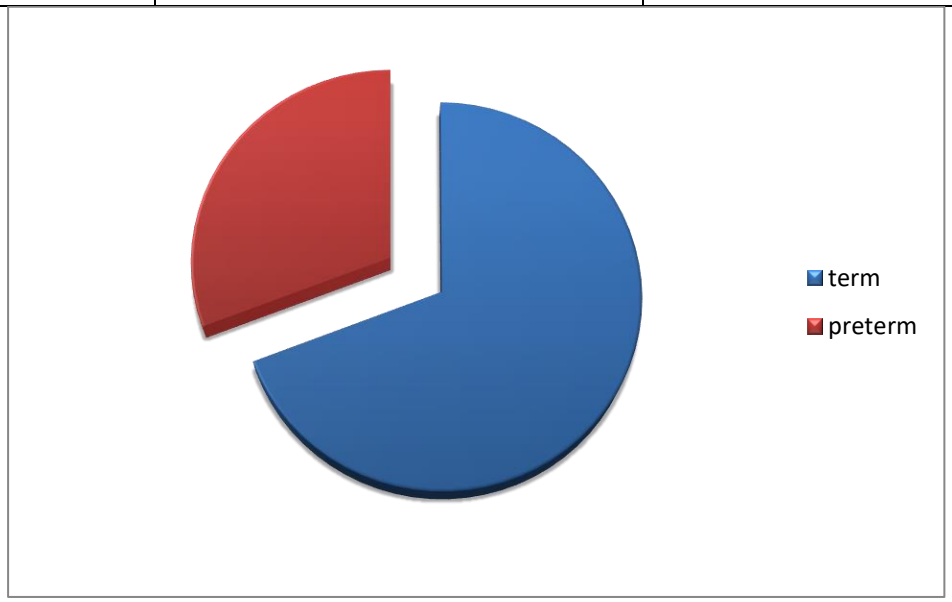
Data Collection:

- All the neonates with seizures are considered for the study, who are fulfilling both inclusion and exclusion criteria, consent was taken from the parents.
- Printed proforma were used for taking the detailed history and all the clinical examination of the neonates including both inborn and out born in Pravara institute of medical sciences, Loni

RESULTS:

Term And Preterm Affected With Neonatal Seizures

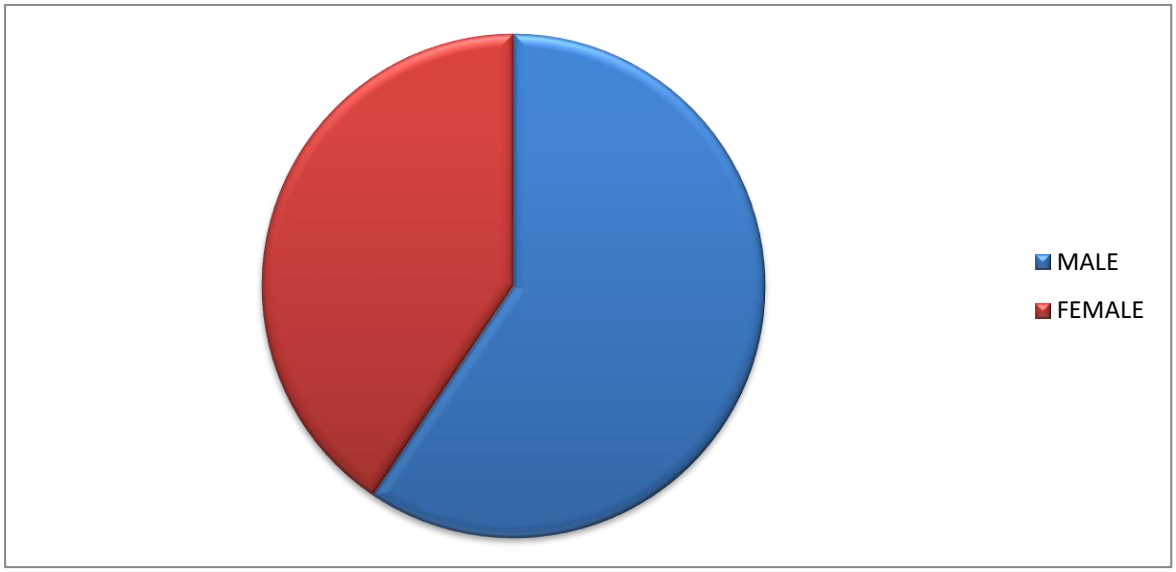
Status	Frequency	Percentage
Term	73	68.8%
Preterm	33	31.1%



Male and females affected with neonatal seizures:

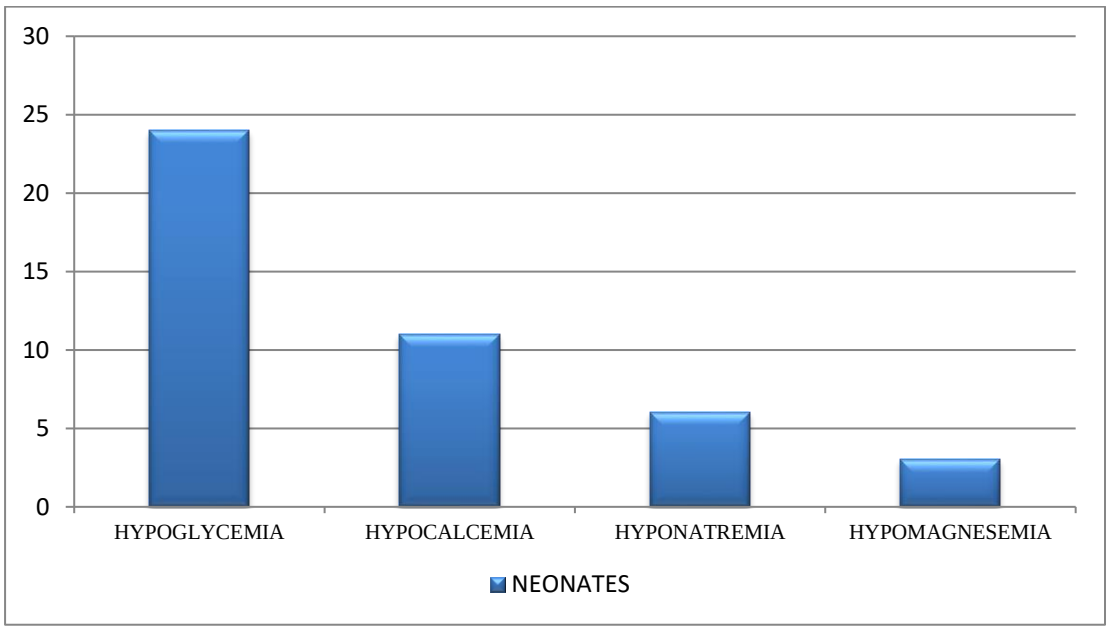
Gender	Frequency	Percentage
Male	63	59.4
Female	43	40.5

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025



Metabolic abnormalities associated with neonatal seizures:

METABOLIC DISTURBANCE	FREQUENCY & PERCENTAGE
HYPOGLYCEMIA	22 (57.8%)
HYPOCALCEMIA	9 (23.6%)
HYPONATREMIA	5(13.15%)
HYPOMAGNESEMIA	2 (5.26%)

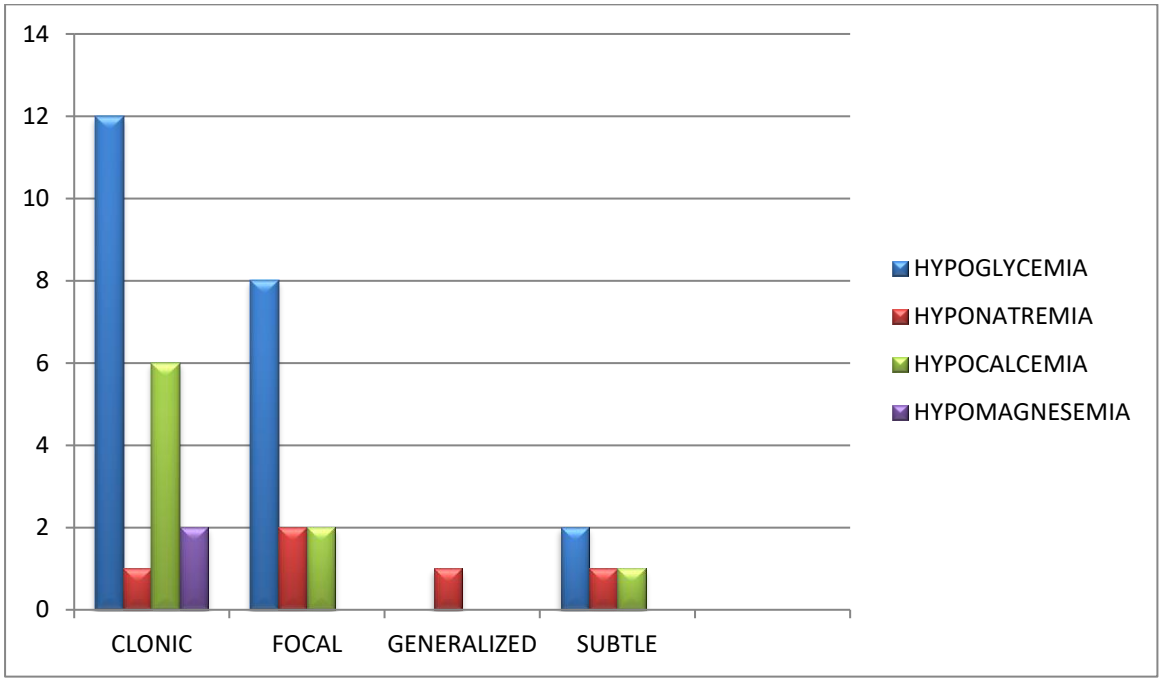


Metabolic Abnormalities Of Various Seizures:

Type of Seizure	Hypoglycemia	Hyponatremia	Hypocalcaemia	hypomagnesaemia
CLONIC	12	1	6	2
FOCAL	8	2	2	0

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

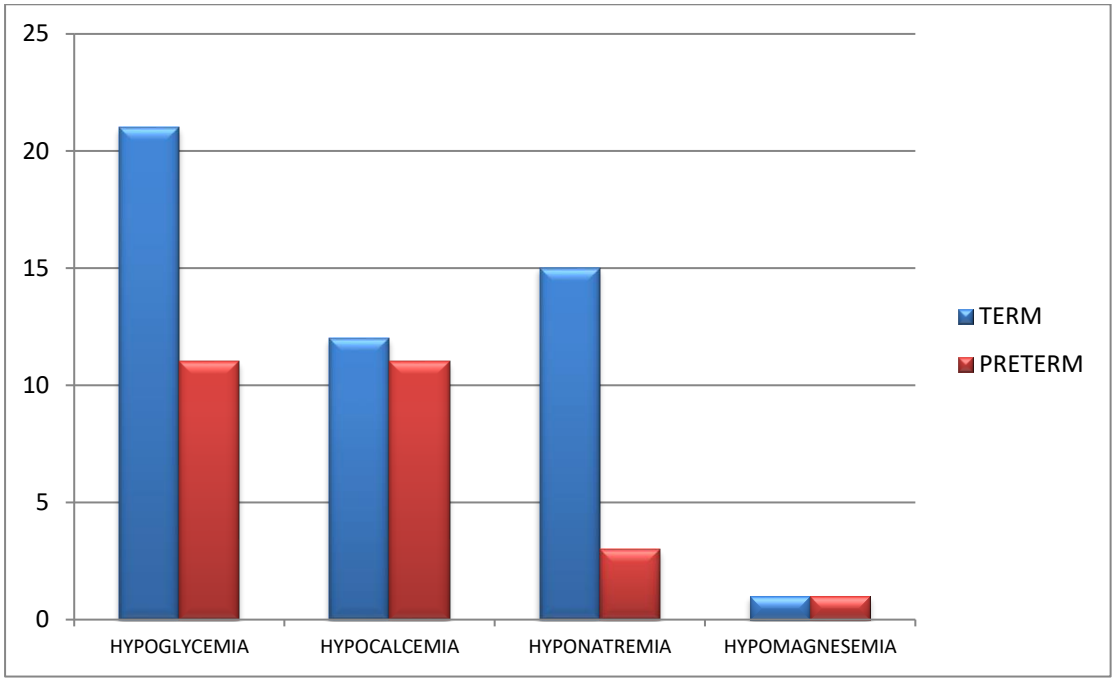
GENERALIZED	0	1	0	0
SUBTLE	2	1	1	0



Term and preterm neonates with seizures with various metabolic abnormalities:

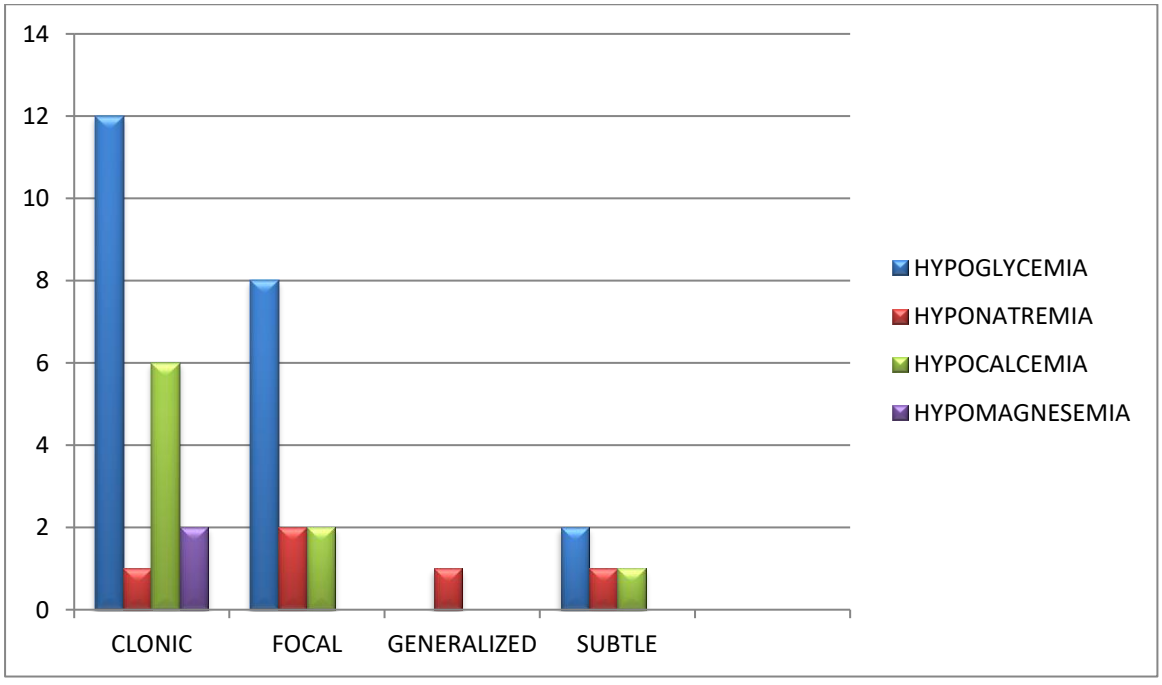
METABOLIC ABNORMALITY	FREQUENCY (TERM)	FREQUENCY (PRETERM)	P VALUE
Hypoglycemia	12 (31.5%)	10 (26.3%)	0.0032
Hypocalcaemia	5 (13.15%)	4(10.52%)	0.0041245
Hyponatremia	5 (13.15%)	0	0.000
Hypomagnesaemia	1 (2.63%)	1 (2.63%)	0.0045

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025



METABOLIC ABNORMALITIES OF VARIOUS SEIZURES:

Type of Seizure	Hypoglycemia	Hyponatremia	Hypocalcaemia	hypomagnesaemia
CLONIC	12	1	6	2
FOCAL	8	2	2	0
GENERALIZED	0	1	0	0
SUBTLE	2	1	1	0



DISCUSSION:

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

Out of 106 neonates with seizures, in our study 55.6% newborns (n=59) were born by normal vaginal delivery and 44.3% (n= 47) were born by caesarean section

In study by Reddy et al 44 neonates (52%) babies were born by vaginal delivery and 40 babies (47%) born by LSCS.

Our study also shows more percentage of deliveries by vaginal mode of delivery. In study by Almuqbil et al 62.2% were born by LSCS and 36.6% were born by NVD. In study by Rastogi et al, 51.6% were born by LSCS and 48.3% were born by NVD. Study by Verma et al didn't mention about the mode of delivery.

COMPARISON OF MODE OF DELIVERY IN NEONATAL SEIZURES AMONG VARIOUS STUDIES:

	LSCS	NVD
PRESENT STUDY	**44.3%**	**55.6%**
RASTOGI ET AL	51.6%	48.3%
REDDY ET AL	47%	52%
ALMUQBIL ET AL	62.2%	36.06%

Out of preterm babies 33.33% were delivered by normal vaginal delivery (n=11) and 66.66% babies were delivered by caesarean section (n=22).

Out of term babies 67.1% were delivered by normal vaginal delivery (n=49) and 32.8% babies were delivered by caesarean section (n=24).

In our study out of 106 neonates, 69.8% were full term neonates (n=74); and 30.1% were preterm neonates (n=32) with statistical significance ($p < 0.05$)

In study by Rastogi et al, out of 63 neonates 85% were term (n=54) and 14.2% were preterm (n=9).

In study by Verma et al 56.93% were term and 41.08% were preterm ; which is also similar to our study.

COMPARISON OF TERM AND PRETERM IN NEONATAL SEIZURES AMONG VARIOUS STUDIES:

	TERM	PRETERM
PRESENT STUDY	69.8%	30.19%
RASTOGI ET AL	85%	14.2%
VERMA ET AL	56.93%	41.08%

Out of 106 neonates, 59.4% were males (n=63) and 40.5% were females (n=43).

In study by Verma et al, 72.27% were males and 27.27% were females.

In study by Rastogi et al, 73.3% were males and 26.6% were females.

In study by Reddy et al, 54.67 % were males and 45.23 % were females.

In study by Rathi et al, 57.5% were males and 42.5% were females, showing similar study findings.

COMPARISON OF MALES AND FEMALES IN NEONATAL SEIZURES AMONGST VARIOUS STUDIES:

	MALE	FEMALE
PRESENT STUDY	59.4%	40.5%

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

VERMA ET AL	72.27%	27.72%
RASTOGI ET AL	71.4%	18.5%
KHER ET AL	56%	44%
REDDY ET AL	54%	46%
RATHI ET AL	57.5%	42.5%

COMPARISON OF METABOLIC ABNORMALITIES ASSOCIATED WITH NEONATAL SEIZURES:

	This study	Rastogi et al	Kumar et al	Verma et al	Reddy at al	Ali et al	Rathi et al
HYPOGLYCEMIA	57.8%	53.5%	52.3%	56%	38.07%	32.7%	51%
HYPOCALCEMIA	23.6%	46.4%	42.8%	26.8%	47.6%	25%	30%
HYPOMAGNESIA	5.26%	-	-	7.3%	14.28%	-	6%
HYPONATREMIA	13.15%	-	-	4.87%	-	42.15%	27%
HYPERNATREMIA	-	-	4.76%	4.87%	-	-	

We further analyzed the type of seizures in these babies.

In hypoglycemic babies, 8.5% babies had subtle seizures, 17.14% babies had tonic seizures, 31.4% babies had clonic seizures.

In hypocalcaemia babies, 5.7% babies had tonic seizures, 17.14% babies had clonic seizures.

In hyponatremic babies, 2.8% babies had subtle seizures, 5.7% babies had tonic seizures, 2.8% babies had clonic seizures, 2.8% babies had generalized seizures.

In hypomagnesaemia babies 5.7% babies had clonic seizures.

In study by Rastogi et al, 25% hypoglycemic babies are with subtle seizures, 17.8% babies had clonic seizures, 10.71% clonic seizures.

In hypocalcaemia babies, 28.5% babies had subtle seizures, 10.71% babies had tonic seizures, 3.57% babies had clonic seizures and generalized seizures each.

In study by Verma et al, in hypoglycemic babies, 26.9% babies had subtle seizures, 3.84% had clonic seizures.

In hypocalcaemia babies 50 % babies had subtle seizures, 19.23% had clonic seizures.

In study by Kher et al, In hypoglycemic babies, 9.9% babies had subtle seizures, 5.9% had tonic seizures, 32.6% babies had clonic seizures, 4.95% babies had generalized seizures.

In hypocalcaemia babies, 19.8% babies had subtle seizures, 1.98% had clonic seizures, 3.96% had generalized seizures.

In hyponatremic seizures, 7.92% had subtle seizures, 5.94% had tonic seizures, 0.99% had generalized seizures.

CORRELATION BETWEEN METABOLIC CAUSE AND TYPE OF SEIZURE:

	SUBTLE	TONIC	CLONIC	GENERALIZED
RASTOGI ET AL				
HYPOGLYCEMIA	25%	17.8%	10.71%	0
HYPOCALCEMIA	28.5%	10.71%	3.57%	3.57%
VERMA ET AL				
HYPOGLYCEMIA	26.9%	0	3.84%	0
HYPOCALCEMIA	50%	0	19.23%	0
KHER ET AL				
HYPOGLYCEMIA	9.9%	5.9%	32.6%	4.95%

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

HYPOCALCEMIA	19.8%	0	1.98%	3.96%
HYPONATREMIA	7.92%	5.94%	5.94%	0.99%
MY STUDY				
HYPOGLYCEMIA	8.5%	17.14%	31.4%	0
HYPOCALCEMIA	0	5.7%	17.14%	0
HYPONATREMIA	2.8%	5.7%	2.8%	2.8%
HYPOMAGNESEMIA	0	0	5.7%	0

In our study clonic seizure is the commonest type of seizure in both hypoglycemic and hypocalcaemia patients, as mentioned in the literature

In our study out of term babies, 31.5% had hypoglycemia (n=12), 13.15% had hypocalcaemia (n=5), 13.15% had hyponatremia (n=5), 2.63% had hypomagnesaemia (n=1).

Out of preterm babies, 25.3% had hypoglycemia (n=10), 10.5% had hypocalcaemia (n=4), 2.63% hypomagnesaemia (n=1).

CONCLUSION:

Our study on neonatal seizures showed male predominance. Most of them born by normal vaginal delivery with term gestation with low birth weight. Most common metabolic abnormality is hypoglycemia. Most common types of neonatal seizures in metabolic abnormality is clonic type followed by subtle seizure. Hence prompt diagnosis and treatment is key to the better survival. The long term follow up with serial neurological examination and developmental assessments is essential to know the final outcome of neonatal seizures.

REFERENCES

1. Mesotten D, Joosten K, van Kempen A, Verbruggen S. ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Carbohydrates. *Clin Nutr* (2018) 37:2337–43. doi: 10.1016/j.clnu.2018.06.947
2. Mergenthaler P, Lindauer U, Dienel GA, Meisel A. Sugar for the brain: the role of glucose in physiological and pathological brain function. *Trends Neurosci* (2013) 36:587–97. doi: 10.1016/j.tins.2013.07.00
3. Suh SW, Hamby AM, Swanson RA. Hypoglycemia, brain energetics, and hypoglycemic neuronal death. *Glia* (2007) 55:1280–6. doi: 10.1002/glia.20440
4. Bentsen MA, Mirzadeh Z, Schwartz MW. Revisiting How the Brain Senses Glucose-And Why. *Cell Metab* (2019) 29:11–7. doi: 10.1016/j.cmet.2018.11.001
5. Dunn-Meynell AA, Routh VH, Kang L, Gaspers L, Levin BE. Glucokinase is the likely mediator of glucosensing in both glucose-excited and glucose-inhibited central neurons. *Diabetes* (2002) 51:2056–65. doi: 10.2337/diabetes.51.7.2056
6. Routh VH. Glucose-sensing neurons: are they physiologically relevant? *Physiol Behav* (2002) 76:403–13. doi: 10.1016/s0031-9384(02)00761-8
7. Alvarsson A, Stanley SA. Remote control of glucose-sensing neurons to analyze glucose metabolism. *Am J Physiol Endocrinol Metab* (2018) 315:E327–39. doi: 10.1152/ajpendo.00469.2017

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 01, 2025

8. McNay EC, McCarty RC, Gold PE. Fluctuations in brain glucose concentration during behavioral testing: dissociations between brain areas and between brain and blood. *Neurobiol Learn Mem* (2001) 75:325–37. doi: 10.1006/nlme.2000.3976
9. Devraj K, Klinger ME, Myers RL, Mokashi A, Hawkins RA, Simpson IA. GLUT-1 glucose transporters in the blood-brain barrier: differential phosphorylation. *J Neurosci Res* (2011) 89:1913–25. doi: 10.1002/jnr.22738
10. Soo JEJ, Ng M, Chong TKL, Tan BKK, Ponampalam R. A case of persistent refractory hypoglycemia from polysubstance recreational drug use. World J Emerg Med. 2023;14(1):75-77. doi: 10.5847/wjem.j.1920-8642.2022.088. PMID: 36713342; PMCID: PMC9842469.
11. Fioramonti X, Chrétien C, Leloup C, Pénicaud L. Recent Advances in the Cellular and Molecular Mechanisms of Hypothalamic Neuronal Glucose Detection. *Front Physiol* (2017) 8:875. doi: 10.3389/fphys.2017.00875
12. Chen BB, Prasad C, Kobrzynski M, Campbell C, Filler G. Seizures Related to Hypomagnesaemia: A Case Series and Review of the Literature. Child Neurol Open. 2016 Jan-Dec;3:2329048X16674834.
13. Farrar HC, Chande VT, Fitzpatrick DF, Shema SJ. Hyponatremia as the cause of seizures in infants: a retrospective analysis of incidence, severity and clinical predictors. Ann Emerg Med.1995;26(1):42-48.
14. Sood A, Grover N, Sharma R. Biochemical abnormalities in neonatal seizures. Indian J Pediatr. 2003;70(3):221-24.