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Clinical profile of hypocalcaemia in term neonates with birth asphyxia in RIMS, Imphal

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ABSTRACT:
Background:Early onset neonatal hypocalcemia is fairly common and seen in first 3-4 days of life in case of prematurity due to early termination of trans-placental supply, exaggeration of the postnatal drop to hypocalcemic levels, increased calcitonin and diminished target organ responsiveness to parathyroid hormone,and in Infant of diabetic mother(may be due to increased calcium demands of a macrosomic baby).In perinatal asphyxia delayed introduction of feeds, increased calcitonin production, increased endogenous phosphate load, renal insufficiency, and diminished parathyroid hormone secretion may contribute to hypocalcemia.
Aims and objectives: To determine the incidence, clinical features and short-term outcome of hypocalceamia in term neonates with birth asphyxia.
Materials and Methods:Prospective longitudinal study carried out in Paediatric Department, RIMS, Imphal during a period of two years (Aug. 2018-July 2020) with approval from Research Ethics Board. Sample size was 236 based on purposive sampling.Pre-designed pro-forma was used for complete clinical history, clinical examination and investigations. Blood was collected for sepsis screening and blood culture and sensitivity. Analysis was done using SPSS v21 for Windows.
Results: Birth asphyxia is a significant risk factor for hypocalcaemia (17.1%). Among neonates having APGAR score 0-3 (46 neonates), 24 neonates (52.17%) developed hypocalcaemia while among neonates having APGAR Score 4-6 (125 neonates) and >6 (65 neonates), 13 neonates (10.4%) and 4 neonates (6.1%) developed hypocalcaemia respectively. These finding were found to be statistically significant ($p < 0.05$.).
Conclusion: Birth asphyxia is a significant risk factor for hypocalcaemia. The other risk factors noted were infant of diabetic mothers, formula feeding, neonates receiving bag and mask ventilation. Seizure was found most common sign/symptoms.Hypocalcaemia should be anticipated in neonates with birth asphyxia, and a timed intervention is required, thereby preventing the complication and succeeding in giving a healthy newborn in the hands of future for everything it needs.
Keywords: Birth asphyxia, hypocalcaemia, term neonate.

I. INTRODUCTION

The World Health Organization (WHO) defines birth asphyxia "failure to initiate sustained breathing at birth".As per AAP (American Academy of Pediatrics) and ACOG (American College of Obstetrics and Gynecology), all the following must be present for designation of asphyxia (a) profound metabolic or mixed acidemia (pH<7) in umbilical cord. (b) persistence of Apgar scores 0-3 for longer than 5 min (c) neonatal neurological sequelae(e.g. seizures, coma, hypotonia) (d) multiple organ involvement (kidney, lungs, liver, heart, intestine).[1]

According to WHO, 4 million deaths per year occur causes related to birth asphyxia which is the largest cause of under 5 mortality (8.5%) after neonatal infections and other complications after birth.[2] Among the neonatal mortality 23% of all deaths are caused by birth asphyxia.[3]

Calcium is maintained within a fairly narrow range from 8.5 to 10.5mg/dl (4.3 – 5.3 Meq/L or 2.2 – 2.7mmol/L). Hypocalcemia is defined as total serum calcium of less than 7 mg/dL (1.75 mmol/L) or ionized calcium less than 4 mg/dL (1 mmol/L).[4]

Early onset neonatal hypocalcemia is fairly common and seen in first 3-4 days of life in case of prematurity due to early termination of trans-placental supply, exaggeration of the postnatal drop to hypocalcemic levels, increased calcitonin and diminished target organ responsiveness to parathyroid hormone,and in

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Infant of diabetic mother(may be due to increased calcium demands of a macrosomic baby). In perinatal asphyxia delayed introduction of feeds, increased calcitonin production, increased endogenous phosphate load, renal insufficiency, and diminished parathyroid hormone secretion may contribute to hypocalcemia.[5]

II. MATERIAL AND METHODS

Prospective longitudinal study carried out in Paediatric Department, RIMS, Imphal during a period of two years (Aug 2018-July 2020) to determine the incidence, clinical features and short-term outcome of hypocalceamia in term neonates with birth asphyxia.

Study design: A hospital based prospective longitudinal study

Study setting: Department of Paediatrics, RIMS, Imphal

Study duration: 2 years (Aug 2018-July 2020)

Study population: All term newborns with birth asphyxia admitted in the Paediatric ward, RIMS Hospital, Imphal during the study period fulfilling the inclusion and exclusion criteria.

Inclusion criteria:

1. The documentation of intrapartumfetal distress through recognition of abnormal fetal heart rate patterns with or without passage of meconium.
2. The presence of immediate neonatal distress as evidenced by a low minute (< 7) Apgar score.
3. The need for immediate neonatal resuscitation including bag and mask ventilation.
4. An abnormal neurologic examination during the first 24 hours of life as judged by application of Sarnat and Sarnat staging.

A full-term newborn fulfilling the above-mentioned criteria will be included in the study

Exclusion Criteria:

1. All neonates with evidence of septicemia, intrauterine infection, congenital anomalies, necrotizing enterocolitis, and marked respiratory distress were excluded from the study.
2. Parents or legal guardian refusing consent

Sample size: 236 by assuming the prevalence of hypocalcemia among asphyxiated neonates is 21.1% (Azam H et al[6])

Sampling method: Purposive sampling.

Procedure methodology:

Term newborn admitted in the inpatient Paediatrics ward with birth asphyxia in Paediatric ward, RIMS according to the inclusion and exclusion criteria was enrolled in the study after informed consent.

A complete history workup, examination and investigations was done according to proforma for all babies.

On the basis of the results of the serum calcium level of term newborn with birth asphyxia prevalence was seen.

Study tools and instruments:

1. **Pre-designed proforma**for complete clinical history, clinical examination and investigations.
2. **Weighing machine**- Electronic weight machine maximum capacity 20kg (d=10gm), KONIG KN-BS10 made in China.
3. **Infantometer**- Indosurgical product. Product code 20014. Made in India.
4. **Glucometer**- One touch select simple blood glucose meter. Lifescan Europe. Made in Switzerland.
5. **Stethoscope**- Littmannquality, 113H39682, Made in USA.

Sample collection:

After all aseptic and antiseptic precaution, sample was collected in sterile container by venepuncture. It was send immediately to Biochemistry Department, RIMS, Imphal for serum calcium level.

Study variables:

Independent/ Predictor variables: Age of the neonate (days), Gender of the neonate, APGAR Score, Maternal Diabetes, Type of feeding, Socioeconomic status, Maternal use of AED, Bag and mask ventilation.

Dependent/ Outcome variables

- Incidence of neonates with hypocalceamia
- Association of hypocalceamia with birth asphyxia

Statistical analysis:

Data was entered and analysed using SPSS (IBM) Version 21.0 software for Windows (IBM Corp.in Armonk, NS, USA). Descriptive statistics like Mean, percentage, SD was used. Chi-square test, t-tests used for inferential statistics. P-value of <0.05 was taken as significant.

Ethical issues:

Commencement of the study was started after approval from the Research Ethics Board, RIMS, Imphal and informed consent was obtained from the parents for the study before recruitment. Confidentiality was maintained by limiting the identifying variables to the minimum.

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III. RESULTS

A hospital based prospective longitudinal study was conducted in the Department of Paediatrics, RIMS, Imphal, from August2018 to July 2020. A total of 236 term neonates with birth asphyxia admitted in the Paediatric ward were included in our study.

Table no 1shows that majority (60.6%) of neonates in the study belonged to male sex.

Table no 1: Sex distribution of participants

Gender	Frequency	Percentage
Male	143	60.6
Female	93	39.4
Total	**236**	**100**

Figure no 1 shows that majority of neonates in study population are less than 4 days old (95.3%).

Figure no 1: Pie chart showing age distribution of participants

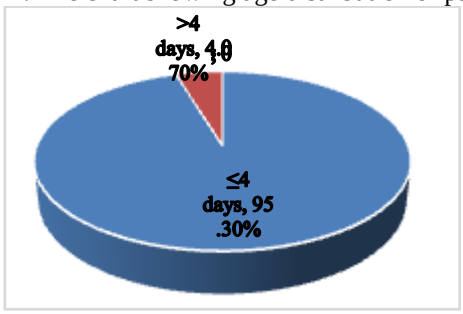

Figure no 2 shows that most of the neonates, 125 (53%) were having APGAR score between 4-6 and 19.5%neonates were having severe birth asphyxia (APGAR score 0-3).

Figure no 2: Bar diagram showing APGAR Score at birth

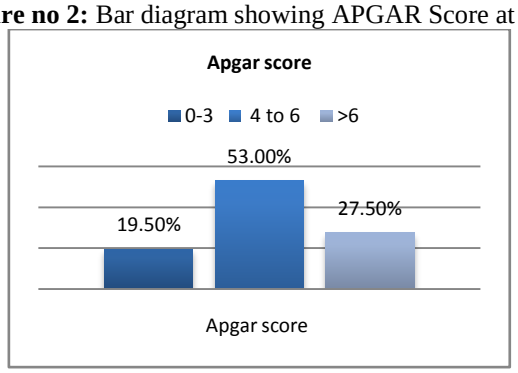

Table no 2shows that among the total 236 recruited into the study, majority (77.5%) received bag and mask ventilation.

Table no 2: Distribution of bag and mask ventilation among participants (N=236)

Bag and mask ventilation	Frequency	Percentage
Received	183	77.5
Not Received	53	22.5
Total	**236**	**100**

Figure no 3 shows that majority (91.5%) of the neonates in the study were born to non diabetic mothers.

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Figure no 3: Distribution of neonates born to diabetic mother

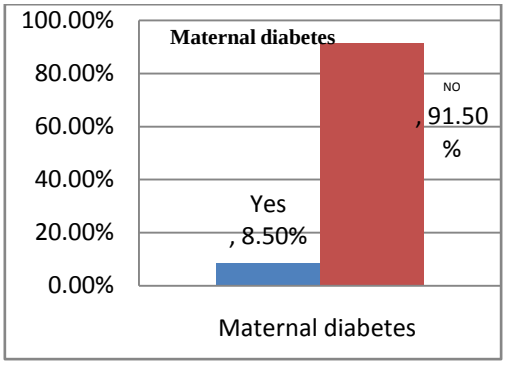

Table no 3 shows that among the total of 236 neonates who constituted the study population, majority (82.6%) had normal S. Ca (more than 8 mg/dl).

Table no 3: Total Serum Calcium distribution among participants (N=236)

Total Serum Calcium	**Frequency**	**Percentage**
>8	195	82.6
≤8	41	17.4
Total	**236**	**100**

Figure no 4depicts thatmajority (83%) of term neonates with birth asphyxiahad normal serum calcium, whereas 17.4% of term neonates with birth asphyxia developed hypocalcaemia.

Figure no 4: Incidence of hypocalceamia in term neonates with birth asphyxia

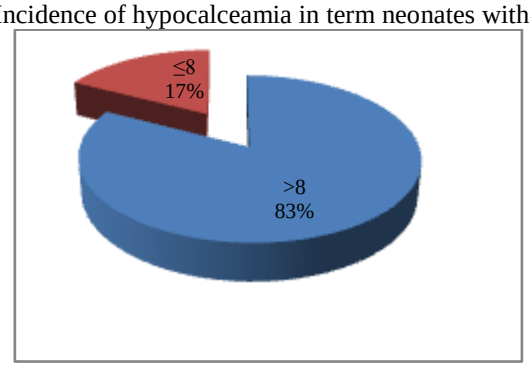

Table no 4 shows that among neonates having APGAR score 0-3 (46 neonates), majority (52.17%) developed hypocalcaemia, while among neonates with higher APGAR scores (4 to 6, and >6), majority had normal serum calcium levels. These finding were found to be statistically significant (p <0.05) showing association between severe birth asphyxia and hypocalcaemia.

Table no 4: Association between total Serum calcium level and APGAR score at birth

Apgar score	**Frequency(N)**		**P value**
	S.Ca>8	**S.Ca ≤8**	
0-3	22	24	0.001
4-6	112	13	
>6	61	4	

Table no 5shows that majority(90.2%) of neonates with hypocalceamia received bag and mask ventilation . These findings were found to be statistically significant (p <0.05).

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Table no 5: Association between Bag and mask ventilation and S.Ca

Bag and mask ventilation	Total serum calcium (mg/dl)		P value
	>8	≤8	
Yes	146	37	0.038
No	49	4	
Total	195	41	

Table no 6shows that majority (60%) of the neonates with hypocalcaemia were born to diabetic mothers, with a statistically significant association between h/o maternal diabetes and hypocalcaemia in neonates.

Table no 6: Association between maternal diabetes and total serum calcium level (N=236)

Maternal Diabetes	Total serum calcium (mg/dl)		P value
	>8	≤8	
Yes	8	12	0.001
No	187	29	

Table no 7shows that among 41 neonates who were hypocalcemic, 34 neonates (82.9%) developed symptoms due to hypocalcemia while none were found symptomatic whose calcium level was more than 8 mg/dl. These findings were found to be statistically significant with p-value <0.05.

Table no 7: Distribution of hypocalcemic neonates by presence of symptoms (N=236)

Total serum calcium (mg/dl)	Symptomatic	Asymptomatic	P value
>8	0	195	0.001
≤8	34	7	

Figure no 5 shows that seizure was found the most common sign/symptom constituting 35.2% followed by jitteriness (20.5%), poor feeding (17.6%), lethargy, irritability and high pitch cry (8.8%) each.

Figure no 5: Distribution of signs and symptoms among hypocalcemic neonates

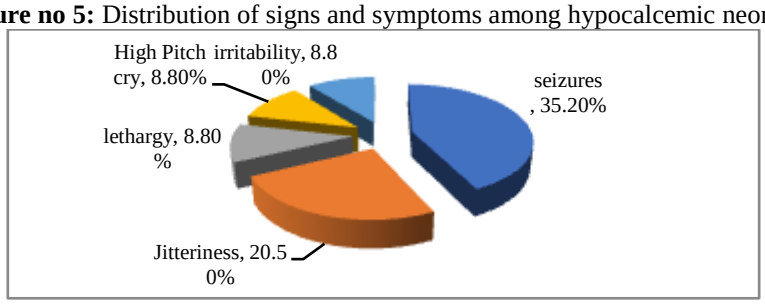
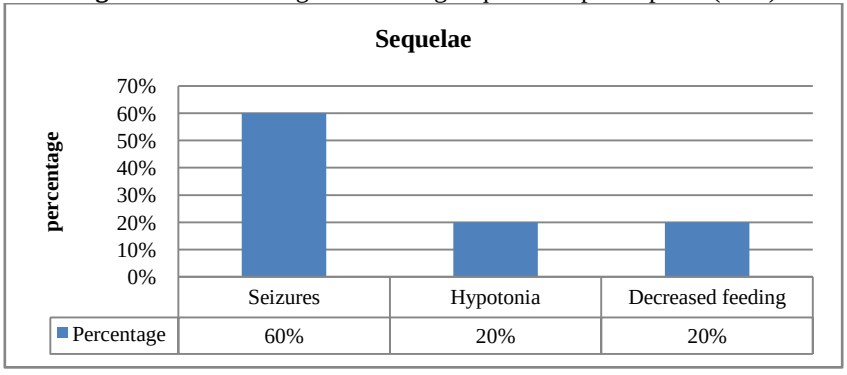


Figure no 6shows that among neonates who developed sequelae most (60%) of them developed seizures on follow up.

Figure no 6: Bar diagram showing sequelae of participants (N=5)



IV. DISCUSSION

Incidence of hypocalcemia in term neonates with asphyxia was found to be 17.4%, which is lower than the incidence found in various prospective studies conducted before,such as the study done by Onyiriuka AN[7] who reported an overall prevalence of 22.6% early-onset neonatal hypocalcaemia among asphyxiated neonates with apgar score 3 or less than 3.

Among neonates having APGAR score 0-3 (46 neonates), majority (52.17%) developed hypocalcaemia, whereas neonates with higher APGAR scores (4 to 6, and >6), majority (91.1%) had normal serum calcium levels. These finding were found to be statistically significant ($p < 0.05$) showing association between birth asphyxia and hypocalcaemia in neonates.

No significant ($p > 0.05$) association could be established between sex and serum Calcium. This finding is similar to study conducted by Khalesi Net al[8].

In our study, majority (90.2%) of neonates with hypocalcaemia (S.Ca <8) are less than 4 days, showing that early onset hypocalcaemia is more common among asphyxiated neonates. This finding is supported by a study conducted by Jain BK et al[9].

A statistically significant association could be established between diabetes in mother and hypocalcaemia in neonates ($p < 0.05$). This finding is supported by study conducted by Azam H et al[10].

A significant ($p < 0.05$) association is observed between type of feeding and serum calcium. Neonates with birth asphyxia on formula feeding were found hypocalcemic (56.4%) than those neonates fed with mother milk (9.6%). These findings were similar to the result of study conducted by Yadav P et al[11].

Majority (82.9%) of neonates with hypocalcaemia was symptomatic in our study, but this is contrary to the study done by Jain BK et al[9] in which only 48% of hypocalceamic infants were symptomatic. The higher incidence of symptomatic infants in our study may be because of other factors such as infants of diabetic mothers, formula feeding which were taken into consideration in our study.

Seizure was found most common sign/symptoms constituting 35.2% follow by jitteriness (20.5%), poor feeding (17.6%), lethargy, irritability and high pitch cry (8.8%) each. This was similar to the study conducted by Onyiriuka AN[7] who also reported that the commonest clinical finding among asphyxiated neonates with early-onset hypocalcaemia was convulsions (57.1%).

Most(64.7%) of the neonates with hypocalcaemia recovered without sequalae. In those neonates who developed sequalae, majority (60%) had seizures on follow up. But this may be also related to birth asphyxia.

V. CONCLUSION

Birth asphyxia is a significant risk factor for hypocalcaemia. The other risk factors noted were infant of diabetic mothers, formula feeding, neonates receiving bag and mask ventilation. Seizure was found most common sign/symptoms. Hypocalcaemia should be anticipated in neonates with birth asphyxia, and a timed intervention is required, thereby preventing the complication and succeeding in giving a healthy new born in the hands of future for everything it needs.

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