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Paediatrics

KEY WORDS: Neonate, Hypoglycemia , Incidence, Neurodevelopment

INCIDENCE OF HYPOGLYCEMIA IN NEWBORN AT RISK AND FOLLOW-UP STUDY OF THEIR NEURODEVELOPMENT AT 3 AND 6 MONTHS AGE

Dr. Rajendra Meher* PostGraduate 3rd Year, Department of Paediatrics Hi-Tech Medical College & Hospital, Bhubaneswar. *Corresponding Author

Dr. Sasmita Devi Agrawal PostGraduate 3rd Year, Department of Paediatrics Hi-Tech Medical College & Hospital, Bhubaneswar.

Dr. Shubhankar Samal PostGraduate 3rd Year, Department of Paediatrics Hi-Tech Medical College & Hospital, Bhubaneswar.

Dr. Sidhant Swarup PostGraduate 3rd Year, Department of Paediatrics Hi-Tech Medical College & Hospital, Bhubaneswar.

Dr. Pankaj Garg PostGraduate 3rd Year, Department of Paediatrics Hi-Tech Medical College & Hospital, Bhubaneswar.

Dr. Hemant Agrawal PostGraduate 3rd Year, Department of Paediatrics Hi-Tech Medical College & Hospital, Bhubaneswar.

ABSTRACT

Background: Glucose is an essential molecule that supplies energy for brain consumption. Neurons and glial cells in the brain are sensitive to hypoglycemia. Thus hypoglycemia may negatively affect neurological and developmental prognosis. **Objective:** This study aimed to investigate the incidence of hypoglycemia in newborn infants at risk & study their neurodevelopment at 3 and 6 months age. **Methods:** The observational study was conducted in babies born with risk factors for hypoglycemia like infant of diabetic mother (IGDM/IDM), LGA (birth weight >90th percentile), SGA (birth weight <10th percentile), late preterm (34-37 weeks). Babies with major congenital malformations ,with perinatal asphyxia, on formula or prelacteal feed and admitted in NICU for other reasons were excluded. The neurodevelopment of these babies (longitudinal study) was evaluated by the DASII scoring method at 3 and 6 months age. **Results:** Of the 142 newborn infants at risk ,there were 15 cases in IDM group (10.56), 32 cases in LGA group (22.53%), 39 cases in SGA group (27.46%), 56 cases in LPI group (39.44`%). The incidence of hypoglycemia in these four groups were 4 (26.67%), 7 (21.87%), 10(25.64%), 17 (30.35%) respectively. Infants at risk having episodes of neonatal hypoglycemia have poor neurodevelopmental outcome (assessed by DASII scoring method) . **Conclusion:** The incidence of hypoglycemia(26.76%) was found to be maximum among LPI group ,followed by IDM group, than SGA group and minimum among LGA group. Long and repeated neonatal hypoglycemia caused poor adaptability.

REVIEW OF LITERATURE

Glucose is an essential molecule that supply energy for brain consumption.Under physiological conditions, the maintenance of normal brain function highly depends on the ATP produced via the continuous supply of glucose; therefore, the transport of glucose into the brain becomes a key step for maintaining cerebral metabolism. Neurons and glial cells in the brain are sensitive to hypoglycemia[1,2] .

Hypoglycemia may be symptomatic in the form of lethargy, irritability, jitteriness, apnea, seizures etc., or may not manifest clinically and be totally asymptomatic. Symptomatic hypoglycemia is associated with poor neurodevelopmental outcome, but the neurodevelopmental outcome of asymptomatic hypoglycemia is uncertain. These asymptomatic hypoglycemic infants should also be treated in view of the possible adverse long-term effects[3,4]. Hypoglycemia often does not produce clinical signs because the newborn brain does not have enough maturity[5] .

The newborns most at risk for, and most frequently screened for, are asymptomatic hypoglycemia include late preterm, LGA, SGA, and/or intrauterine growth restricted (IUGR) infants, and IDMs . Frequent milk feedings with repeated glucose measurements is the current standard treatment for asymptomatic hypoglycemia in these groups of patients[6].

Definition of Hypoglycemia in newborn:
Within the first postnatal 4 hour : Hypoglycemia=blood glucose ≤ 40 mg/dL and Severe Hypoglycemia= blood glucose ≤ 25 mg/dL . # In the postnatal 4h -24 h :- Hypoglycemia= blood glucose ≤ 45 mg/dL and Severe hypoglycaemia= blood glucose ≤ 35 mg/dL # Prolonged hypoglycaemia : the baby is still hypoglycemic after 1 h of intervention, and recurrent hypoglycaemia is more than one hypoglycemic episodes At birth, the blood glucose concentration of newborn is about 70% of the maternal level. It reaches rapidly to a nadir by 1 hour to a value as low as 20 to 25 mg/dl. This nadir and the lower levels of blood glucose are prevalent in all healthy neonates. These levels are transient and begin to rise over the first hours and days of life. This is normal adaptation for postnatal life and it helps to establish postnatal glucose homeostasis.[7,8,9] In 2011 the AAP published clinical guidelines to address some of these concerns, with special attention to management of hypoglycemia in the first 24 h of life. They suggested that late preterm, LGA, SGA/IUGR, and IDM newborns should be fed by one hour of age and have their glucose checked 30 min after the feeding. Glucose monitoring should then continue before feeds through 12 h of age for LGA and IDM patients as long as pre-feed plasma glucose concentrations remain greater than 40 mg/dL (2.2 mmol/L). It was suggested that late preterm and SGA infants should be screened before feeds for 24 h.

KNOWN RISK GROUPS INCLUDE:-

- IDM/IGDM (Infant of diabetic mother) [maternal type 1 or type 2 diabetes mellitus or gestational diabetes mellitus]
- LGA (Large for gestational age) (birth weight >90th percentile)

- SGA (Small for gestational age) (birth weight <10th percentile)
- [LGA & SGA both according to Fenton growth curve]
- Late preterm (34 -36^{6} ^{7} gestational weeks).
- In order to avoid overlapping of patients in grouping, infants of diabetic mother were included in the IDM group regardless of birth weight. Late preterm neonates group was constituted according to gestational age regardless of the babies' SGA or LGA status.

OBJECTIVE

This study aimed to investigate the incidence of hypoglycemia in newborn infants at risk (IDM, SGA,LGA, LPI) and study their neurodevelopment at 3 and 6 months age.

MATERIAL AND METHODS

- **Type of Study:-** Observational study , Longitudinal in nature
- **Place of Study:-** Hi-tech Medical College and Hospital, Bhubaneswar
- **Period of Study:-** January 2018 to August 2019
- **Sample size :-** 142 newborn infants AT RISK
- **Inclusion criteria :** Newborn babies at 'Risk of Hypoglycemia' as described (IDM, SGA ,LGA, LPI)
- **Exclusion criteria :** Babies with congenital mal formations, newborn sufferings perinatal asphyxia, on formula or prelacteal feeds and admitted in NICU for other reasons (sepsis, polycythemia, jaundice, etc).

BLOOD GLUCOSE TESTING

Capillary blood samples were taken from heel of the babies after warming. Blood glucose concentrations were determined using digital glucometer (Dr.Morepen) and test strips. Glucometer was calibrated monthly. If low blood glucose concentration was detected, it was confirmed by laboratory testing. First blood glucose tests in babies were made half an hour after feeding. The babies were fed every 2 hourly for 24 hour and the blood glucose was checked at 2,6,12,24,48 and 72 hours of life, prior to feeding.

NEURODEVELOPMENTAL ASSESSMENT

The neurodevelopment of these babies was evaluated by the (Developmental Assessment scales for Indian Infants) DASII scoring at 3 and 6 months age.

The observed behavior pattern was compared to the corresponding normal behavior with the help of DASII scoring cards. The infant development score was calculated according to the following formula: DQ = CA/AA × 100, where DQ is the developmental quotient, CA is the childbearing age (calculated from the DASII scoring charts), AA is the actual age. Infant development was defined as follows: DQ < 70 is abnormal, DQ = 70–84 is suspected abnormal, and DQ > 85 is normal. During treatment, DQ served as an indicator for the degree of development disorder (DD).

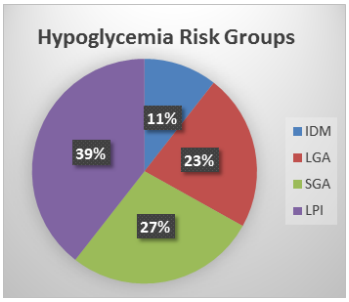
DASII Scoring chart includes (Upto 6 months age) :-

Motor Scales	Mental Scales
Neck control	Visual cognizance
Body control	Auditory cognizance
	Social Interaction
	Reaching and manipulation
	Vocalisation

RESULTS

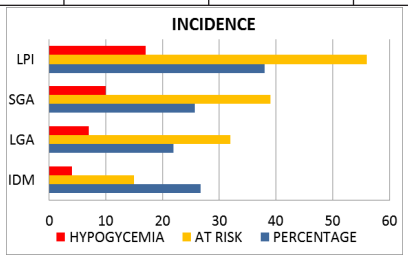
1] Out of the 142 newborn infants at risk for hypoglycemia there were:

- 15 cases in IDM group (10.56%)
- 32 cases in LGA group (22.53%)
- 39 cases in SGA group (27.46%)
- 56 cases in LPI group (39.44%).



INCIDENCE OF HYPOGLYCEMIA:

RISK GROUPS	INCIDENCE	PERCENTAGE	REMARKS
LPI	17 OUT OF 56	30.35 %	HIGHEST
IDM	4 OUT OF 15	26.67 %	
SGA	10 OUT OF 39	25.64 %	
LGA	7 OUT OF 32	21.87 %	LOWEST



DASII SCORING RESULTS

The incidence of hypoglycemia was 38 out of 142 (26.76 %) newborn infants at risk . But for neurodevelopmental assessment at 3 and 6 months age ,we received 23 out of 38 newborn infants that suffer from one or above episodes of hypoglycemia(other were lost to follow up ,some at 3 months and some at 6 months).

DASII SCORING	RESULTS	PERCENTAGE
DASII Score achieved > 85 % (Normal)	7 OUT OF 23	30.43 %
DASII Score achieved 70%-85% (Needs Follow-Up)	11 OUT OF 23	47.82 %
DASII Score achieved < 70% (Needs further Investigation & Treatment)	5 OUT OF 23	21.73 %

DISCUSSION

The incidence of hypoglycemia (26.76%) which was much more compare to other newborn) was found to be maximum among LPI group , followed by IDM group, than SGA group and minimum among LGA group. In this study, 38 infants who had neonatal hypoglycemia (out of 142 newborn infants at risk) were analyzed for their neurodevelopment by the DASII scoring method to investigate their gross motor, visual and auditory cognizance, social interaction, vocalization, reaching and manipulation at 3 and 6 months of age. We found that long and repeated neonatal hypoglycemia affected neurodevelopment (21.73 %) and was associated with a high risk of poor adaptability. Indeed, studies in newborns with hypoglycemia by magnetic resonance imaging have shown that edema occurs in the posterior occipital and cortex region, with symmetrical changes[10,11] . The occipital and cortex regions are somatosensory and visual control areas[12] , which impact cognitive skills, adaptability, and visual skills. Under hypoglycemic conditions, the liver glycogen reserves are insufficient. Once the blood sugar level reaches the lowest point, the synthesis of lipids, proteins, DNA, and RNA is limited or delayed because not enough energy is lied, thus affecting brain cell metabolism and development and eventually leading to neuronal necrosis. A high level of glucose is required for the occipital region because there are more neurons and synapses in this region[13] .If hypoglycemia not able to be quickly corrected,

irreversible brain damage in the posterior occipital and cortex regions will result. Neonatal hypoglycemia is a common metabolic disorder during the neonatal period. Volpe has indicated that continuous, repeated hypoglycemia can cause brain damage[14] . In addition, Filan et al. have found that neonatal hypoglycemia can injure the occipital brain, resulting in long-term disability, visual impairment, and epilepsy[13].

CONCLUSIONS

1. Neonatal hypoglycemia is a common metabolic disorder during the neonatal period especially in the presence of 'Risk factors for Hypoglycaemia'.
2. Hypoglycemia screening should be done at regular interval, more specifically at first 24 hours of life in at Risk Babies where Exclusive Breastfeeding is followed.
3. Long and repeated neonatal hypoglycemia caused poor neurodevelopmental outcome and adaptability to life.

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