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Incidence, age at onset, clinical spectrum and short term outcome of neonatal hypoglycemia in a tertiary care hospital: a prospective cohort study

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Abstract
Objective: To study incidence, age at onset , clinical spectrum and short term outcome of neonatal hypoglycemia
Study design: *Prospective cohort study*
Setting & Participants: Newborns who admitted with high risk for neonatal hypoglycemia at Neonatology Division, Department of Pediatrics, Coimbatore Medical College Hospital, Coimbatore, tertiary care hospital in Tamilnadu.
Methodology:
High risk newborns are screened for hypoglycemia since admission into NICU by point of care glucometer devices which use glucose oxidase-peroxidase method. Blood sugar < = 45 mg/dl taken as cutoff for hypoglycemia. Screening for hypoglycemia done. The incidence of hypoglycemia, different clinical spectrum in specific birth weight and maturity categories and short term neurodevelopmental outcome after hypoglycemia at 3 and 8 months were studied using Denver developmental screening test II.
Results: *the incidence was 3.4 % in high risk population, In our study 65% (n=86) of babies had hypoglycemia in the first 48 hours of life. Mean age at onset of hypoglycemia is 41 hours and more common in term babies. 75 % hypoglycemic babies are small for gestational age and growth restricted . 63% of babies had asymptomatic hypoglycemia , which identified on routine screening. At 8 months of* ***corrected age*** *42 babies had gross motor, 26 had language, 52 had fine motor and 34 had personal social milestones delay.*
Conclusion: *Neonatal hypoglycemia is a serious issue with under diagnosed and poorly follow up neonatal morbidity in paediatric population. Neurodevelopment beyond infancy to be addressed. Asymptomatic hypoglycemia is the most common presentation. Term SGA/IUGR are more prone for hypoglycemia than preterm AGA babies.*
Keywords: *hypoglycemia, neurodevelopment, newborn, morbidity*

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I. Introduction

Neonatal hypoglycemia is common during the hours and days following birth. It may be transitory and asymptomatic but can result in a range of acute symptoms. If sufficiently prolonged, the condition is associated with risk of irreversible neurological (brain) damage. Controversy has always surrounded the precise plasma/blood glucose concentration that should be used to diagnose neonatal hypoglycemia . Currently, the most widely used is plasma glucose <2.5 mmol/L (<45 mg/dL) but is disputed. The overall incidence has been estimated at 1 to 5 per 1,000 live births, but it is higher in at-risk populations. Causes of hypoglycemia vary from genetic, congenital , metabolic, iatrogenic and others include prematurity, IUGR, sepsis, perinatal stress etc.,. asymptomatic hypoglycemia is most common and severity vary from transient to refractory and pronlonged. Although most common in NICU the neurological outcome of them are poorly studied and even unrecognised. Therefore study planned to follow up on their early infantile development.

II. Methodology

Study Design: prospective cohort study
Study Centers: Neonatology Division, Department of Pediatrics, Coimbatore Medical College Hospital, Coimbatore, Tamilnadu ,India
Duration of the Study: March 2018 to February 2019

III. Material & Methods:

Subjects:

The High risk newborns are screened for hypoglycemia since admission into NICU by point of care glucometer devices which use glucose oxidase-peroxidase method. Survival and duration of treatment required for hypoglycaemia is compared and duration of stay is obatained. Those who had symptomatic and refractory hypoglycemia are undergot MRI brain. Neuro developmental outcomes of hypoglycemic babies are followed up using Denver developmental scale II at 3 and 6 months of life.

A. Inclusion Criteria:

a. Preterm infants (<35 weeks)
b. Small for gestational age infants (SGA) : birth weight <10th percentile
c. Infant of diabetic mothers (IDM)
d. Large for gestational age (LGA) infants: birth weight >90th percentile*
e. Infants born to mothers receiving therapy with Terbutaline/Propranolol/Labetalol/oral hypoglycemic agents.
f. Infants with morphological IUGR.
g. Sick neonates with perinatal asphyxia, polycythemia, sepsis.

B. Exclusion Criteria:

a) Term , healthy, breast feed , AGA infants.
b) LGA infants of constitutionally large parents

Procedure/Intervention:

Blood sugar < = 45 mg/dl taken as cutoff for hypoglycemia. Screening for hypoglycemia done at 2, 6,12,24,28,72 hrs and then every 24 hrs upto 7 days of life in high risk babies. Those who had low blood sugar, screening frequency was increased depending upon the blood sugar . Baseline variables and age at onset of hypoglycaemia are recorded. Asymptomatic hypoglycemia with blood sugar 20-45 mg/dl treated with feeding. For symptomatic babies 10% Dextrose bolus followed by glucose infusion rate was started at 6 mg/kg/min. GIR was increased at 2mg/kg/min depending upon the response upto a maximum of 12 mg/kg/min. If blood sugar is not maintained with GIR fluid that corticosteroids are added and Octreotide is added if there is no response to steroids for 24 hours.

Data collection and Monitoring:

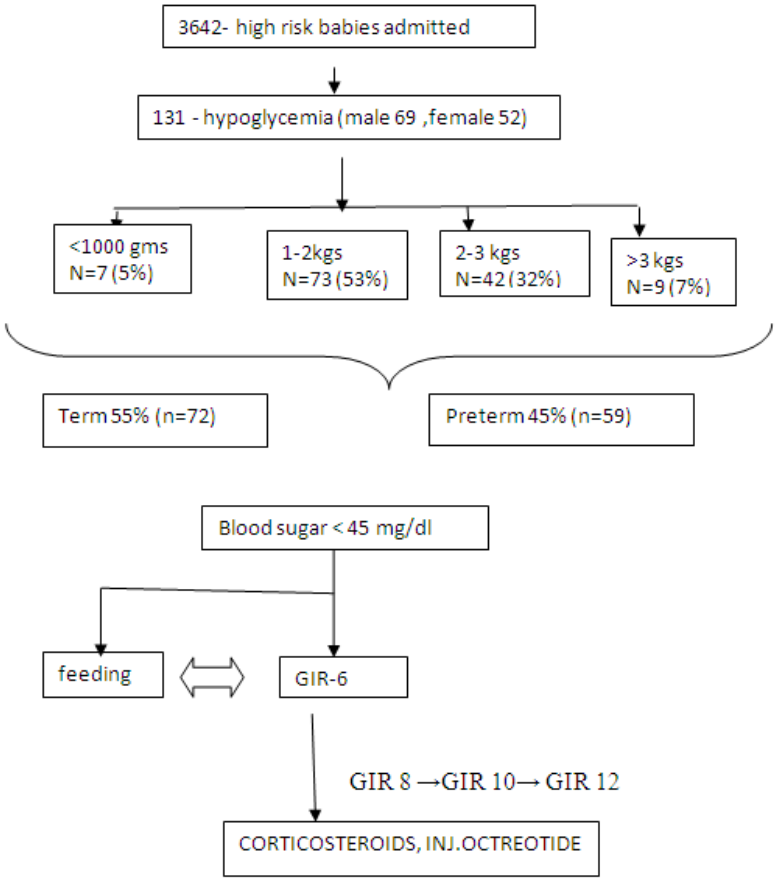
Sample size was calculated assuming incidence of hypoglycemia in NICU was 10%. Neonatal baseline characteristics like birth weight, gender, gestational age, age at onset of hypoglycaemia, symptoms of hypoglycemia and co morbid conditions like sepsis were recorded. Data collection on maternal characteristics included gestational diabetes mellitus, tocolytic drug usage.

Survival and duration of treatment required for hypoglycemia was compared and duration of stay were monitored. Those who had symptomatic and refractory hypoglycemia are underwent MRI brain. Neuro developmental outcomes of hypoglycemic babies followed up using denver developmental scale II at 3 and 8 months of life using corrected age.

IV. Statistical Analysis

The data was analyzed using SPSS 23.0 for Windows. The baseline clinical characteristics and outcome variables were compared with the ANOVA for parametric and Kruskal-Wallis test for non-parametric comparisons of continuous variables, and chi square test for categorical variables.

Study flow:



V. Observations And Results

Incidence

Incidence of hypoglycemia among studied population was found to be 3.6 percentage(n= 131) of total high risk babies(n=3642).

Distribution of birth weight and age at onset of hypoglycemia

55 % (n= 73) of hypoglycemia occurred among 1000- 2000 gm babies. Also 32 %(n=42) of babies were fall between 2000-3000 gms. The prevalence of hypoglycaemia is inversely proportional to the birth weight among high risk babies.

High risk babies mostly go for hypoglycemia with first 48 hours of birth 65%(n=86). Also 30% (n=39) of hypoglycemic events commence with 120 hours of birth. Mean time of onset of hypoglycemia is 41 hours in our study.

Gestational age and co morbid conditions

Hypoglycemic events are more common among term 55%(n=72) than preterm 45%(n=59) neonates.

Hypoglycemia is more common among SGA/IUGR babies 75%(n=98). Also 22 % (n=29)of appropriate for gestational age babies also had hypoglycemia. Only 8.4 %(n=11) babies are being Infant of diabetic Mothers (IDM).

Around 26%(n=35) of high risk babies had underlying sepsis.

Clinical features	outcome		Discharge age		
	survived	died	<5d	6-10d	>10d
<1000 g	5(71.4%)	2(28.6%)	0	0	5(100%)
1-2 kg	67(92%)	6(8%)	6(8%)	33(45%)	28(37%)
2-3 kg	42(100%)	0%	4(9%)	26(62%)	12(29%)
>3kg	8(89%)	1(11%)	3(33%)	4(44%)	1(13%)
P value	0.33		0.004		

Clinical features and course of treatment needed:
Around 27.5% (n=36) babies presented with symptomatic seizures. 9% (n=12) of babies presented with symptomatic feed intolerance , irritable cry, lethargy, apnoea, etc. 63.5% (n=83) of hypoglycemic events were asymptomatic & identified in routine screening.
Around 27.5% (n=36) of (asymptomatic mainly) hypoglycemia are treated with feeding and corrected by feeding itself. 59 % (n=78) of hypoglycemia treated with glucose infusion rate at 6-8 mg/kg/min. 12 % (n=16) babies needed GIR at 10-12 mg/kg/min.
About 21% (n=28) of hypoglycemic babies received steroids for suspected adrenal insufficiency for refractory hypoglycemia. About 16% (n=22) babies octreotide of persistent hypoglycemia.
Duration of treatment and survival:
9 out of 131(7%) babies died during study period because of underlying illnesses/co-morbidities.
Around 42%(n=56) of hypoglycemia needed less than 72 hours of therapy. 47%(n=61) babies needed 4-7 days of treatment for hypoglycemia. 14 babies (11%) babies had persistent hypoglycemia beyond 7 days.
48% (n=63) babies discharged between 6-10 days of admission. 35% (n=46) of babies discharged after more than 10 days of hospital may be due to underlying co-morbidities mainly sepsis. Babies of birth weight between 1000-2000 gms , 92% (n=67) of babies survived and 2-3 kg 100 %(n=42) of babies survived. P value was 0.33 .
Duration of hospital stay:
In 2-3kgs babies 45% (n=33) are discharged between 6-10 days and 37% (n=28) has been discharged after 10days. In babies more than 2 kgs, 62 % (n=26) discharged in 6-10 days. P value is 0.004 .
8 out of 9 babies(89%) of sepsis babies who are hypoglycemic are died.($p< 0.001$.
Sub group analysis between symptoms and duration of treatment needed:
Around 72%(n=26) of hypoglycemic seizures needed hypoglycemia treatment for more than 4 days. About 53%(n=44) of asymptomatic hypoglycemia is transient settles by less than 72 hours. Even other symptomatic hypoglycemia like apnoea, feed intolerance ,lethargy, irritable cry, etc also needed treatment between 4-7 day which is about 58%(n=7). P value is 0.02 .
Also there is strong correlation between symptomatic hypoglycemia and duration of hospital stay. p value is 0.05.

Distribution of developmental domains

DDST II	Gross motor	language	Fine motor adaptive	Personal social
3 months (n=67)	44	22	53	26
8 months(n=62)	42	26	52	34

At 8 months of **corrected age** 42 babies had gross motor, 26 had language, 52 had finemotor and 34 had personal social milestones delay.

VI. Discussion

Neonatal hypoglycemia is common and linked to poorer neurologic outcome. It is a common problem requiring continuous screening and monitoring and can often leads to neurological damage if left untreated. The clinical management of babies at risk of hypoglycemia has also altered over recent decades, with improved identification of babies at risk, improved methods of diagnosis, and a greater focus on early feeding and glucose monitoring.

There are lots of studies available about incidence of hypoglycemia and a few studies regarding neurodevelopmental outcomes.

Incidence of hypoglycemia

Deborah L. Harris and co workers enrolled 514 risk babies and reported that 51% became hypoglycemic among high risk babies like late preterm, SGA,IDM and LGA. Of that 19% had severe hypoglycemia , and 19% had more than 1 episode. The incidence and timing of hypoglycemia was similar in all at risk groups, but babies with a total of 3 risk factors were more likely to have severe hypoglycemia. In our study , 3642 high risk babies who fulfill inclusion criteria were screened , of which 131 babies had hypoglycemia which is about 3.4%. Out of 371 IDM babies admitted , only 11 (8.5%) babies had hypoglycemia , which is about 3%.

Age at onset

Deborah L. Harris et al reported onset of hypoglycemia more common at first 24 hours of life. In our study 65% (n=86) of babies had hypoglycemia in the first 48 hours of life. Mean age at onset of hypoglycemia is 41 hours in our study.

Maturity and birth weight comparison

In Orhideja Stomnaroska1 et al study of hypoglycemia in newborn, the birth weight was dominated by children with low birth weight: very low birth weight (VLBW)(<1500g) 253 children, (34,23%), low birth weight (1500-2500g) 402 (54.39%), appropriate for gestational age (AGA) 78(10.55%), and high birth weight (>4000g) 6 babies (0.81%).

In our study, 56 % babies between 1-2 kgs and 32 % between 2-3 kgs. 55 % of babies are term neonates and 45 % are preterm babies.

75 % hypoglycemic babies are small for gestational age and growth restricted. 3% of hypoglycemic babies are Large for gestational Age.22% babies are AGA .

There is significant association Between birth weight and survival in neonatal hypoglycemia p value < 0.05.

There is significant association Between birth weight and discharge age in neonatal hypoglycemia. As the birth weight increases duration of hospital stay decreases. p value < 0.05.

There is significant association Between maturity (AGA,SGA, LGA) and discharge age in neonatal hypoglycemia. SGA babies have increased duration of hospital stay. p value < 0.05.

Clinical manifestations of hypoglycemia:

In Orhideja Stomnaroska et al study, Asymptomatic hypoglycaemia was found in 550 (25.57%) children, while symptomatic hypoglycemia with seizures was observed in 189 (74.43%). In our study 27% of babies had hypoglycemic seizures as first manifestation. 63% of babies had asymptomatic hypoglycemia , which identified on routine screening. 10 % babies were presented with apnoea, feed intolerance, lethargy irritable cry, jitteriness as the features of hypoglycemia. IDM babies had less hypoglycaemia in our study

Babies who had transient asymptomatic hypoglycemia, responded with feeding of breast milk as Expressed breast milk only. Most of the symptomatic babies required higher glucose infusion rates with increased duration of treatment and long duration of hospital stay. Prolonged hospital stay also common with co morbidities like sepsis, prematurity, very low birth weight , etc .

We analyzed the relation of various demographic factors and risk factors of hypoglycemia on neurodevelopmental outcome. In our study no statistically significant difference in prevalence of neurodevelopmental outcome was observed ($p>0.05$) at any stage of follow up between male and female neonates. Chandrashekaran et al. did not found any significant association with gender, similar to our study. Although the prevalence of neurodevelopmental abnormalities was more in low birth weight babies than normal birth weight babies with hypoglycemia in our study but it was not statistically significant

In our study, we noticed high prevalence of abnormal neurodevelopment in neonates presented late in their life. In our study, there is significant relationship of age of presentation and neurodevelopmental outcome [$p<0.05$].

VII. Conclusion

This prospective observational study found a high prevalence of adverse neurodevelopmental outcome in neonates with hypoglycemia. Factors such as duration of hypoglycemia, presence of symptoms, Gestaional age, birth weight, higher GIR requirement were significantly associated with adverse neuro developmental outcome as assessed by Denver Developmental Screening Test II (DDST II). In new-born infants, low blood glucose levels lead to neuronal and glial cell death, and hence associated with long-term neurodevelopmental handicaps. Early diagnosis and treatment of neonatal hypoglycemia is mandatory to prevent the longterm neurological sequelae.

References:

[1]. Aynsley-Green A. Glucose, the brain, and the pediatric endocrinologist. *Horm Res.*1996;46:8–25
[2]. Kalhan S, Saker F. Metabolic and endocrine disorders, part one: disorders of carbohydrate metabolism. In: Fanaroff AA, Martin
[3]. RJ, eds. *Neonatal-Perinatal Medicine:Diseases of the Fetus and Newborn*. 6th ed. St. Louis, Mo: Mosby-Year Book Inc; 1997
[4]. Stanley CA. Hyperinsulinism in infants and children. *Pediatr Clin North Am.*1997;44:363–374
[5]. Williams AF. *Hypoglycemia in the Newborn: A Review*. WHO Publications #5778, 1997
[6]. Clohearty manual on neonatology 18th edition
[7]. Chandrasekaran A, Rao PNS, Raman V, Nesargi S, Shekharappa CB, et al.(2016) Glucose levels in first 3 days and neurodevelopmental outcome at 1 year in low birth weight infants: A cohort study. Indian J Child Health. Pp: 274-280.
[8]. Neurodevelopmental Outcome in Neonates with Hypoglycaemia and Associated Risk Factors: Melana1, Nishat Ahmed1, Rajendra Kumar Soni1 and Manu Goyal. Melana et al., J Preg Child Health 2017, 4:3 ,DOI: 10.4172/2376-127X.1000323

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