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Original Research Paper

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A STUDY TO ASSESS INCIDENCE, RISK FACTORS, COMPLICATIONS OF HYPOGLYCEMIA AND ITS OUTCOME IN NEWBORNS ADMITTED IN A TERTIARY HEALTH CARE CENTRE

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ABSTRACT

Background: Current screening guidelines and management of hypoglcemia are based on limited evidence and rely more on expert judgement to make recommendations. In this study we aimed to study the incidence of hypoglycemia in newborns with risk factors and the possible outcome of newborn born with neonatal hypoglycemia was also assessed. **Material and Method:** This Cross-sectional Observational study was conducted on 100 babies born in IMCHRC with risk factors for hypoglycemia qualifying the inclusion criteria. Hypoglycemia screening was done at 1,2, 6, 12, 24 and 48 hours of life. Blood sugar was screened with hypoglycemia defined as RBS <45 mg/dl. Statistical analysis was done. **Results:** The incidence of hypoglycemia in newborns with risk factors was 36% with majority neonates being asymptomatic. Males and Pre-term neonates showed a higher prevalence to develop hypoglycemia. Majority of hypoglycemic newborns were SGA and birthweight was <2 kg. Preterm neonates developed hypoglycemia much earlier than term & post term mostly by 2 hours of life. Preeclamsia was the most common maternal risk factor and Prematurity the most common fetal risk factor that causes hypoglycemia in high-risk neonates (P>0.05). 4 newborns succumbed to death out of which 3 were Pre-Term and 1 was Term. **Conclusions:** Hypoglycemia screening should be done at regular interval, more specifically at first 24 hours of life in at-risk babies. Proper monitoring of hypoglycemia, majority of the newborns will recover though adequate feeding practices and will decrease chances of giving invasive treatment.

KEYWORDS : Hypoglocemia, Clinical profile, Risk factors, Neonates, Prevalence

INTRODUCTION

Neonatal hypoglycemia has been recognized for many years, although with time there have been wide swings of opinion regarding the definition of the condition, its clinical significance & its optimal management.[1] The reported incidence of hypoglycemia varies with its definition, but it has been estimated to occur in approximately 16% of large-for-gestational-age (LGA) infants & 15% of small-for-gestational-age (SGA) babies.[2]

Blood-glucose levels are frequently lower in newborn babies than in older children or adults, but confirming a diagnosis of clinically significant hypoglycemia requires that one interpret the blood glucose level within the clinical context.[2] There is no precise plasma/blood glucose. concentration that should be used to diagnose neonatal hypoglycemia. The AAP has arbitrarily adopted the numerical plasma glucose value of 47 mg/dL (2.6 mmol/L) to define hypoglycemia in neonates.[3] WHO defined hypoglycaemia as blood glucose level less than 45 mg/dl.[4]

Neonatal hypoglycemia can occur due to various causes like congenital hyperinsulinism, asphyxia, hypothermia, prematurity, septicemia, congenital hypothyroidism, inborn errors of metabolism, etc. The clinical spectrum of hypoglycaemia is not specific.

It can be symptomatic or asymptomatic, with asymptomatic being the most common type. Symptoms are convulsion, lethargy, hypotonia, apnea, poor feeding, irritability, high pitched cry, cyanosis and are nonspecific and can be missed easily especially in sick neonate.[5-7] Hypoglycemia can also be further classified as transient or persistent hypoglycemia.

Neonatal hypoglycaemia can be easily treated if recognized early. The clinical signs and symptoms should improve with correction of low glucose concentration. Most cases of neonatal hypoglycemia are transient, respond readily to treatment and are associated with an excellent prognosis. Untreated hypoglycaemia whether symptomatic or asymptomatic results in neurological impairment and mental retardation of varied severity.[8,9]

Hypoglycemia is one of the most common metabolic problems seen in both the newborn nursery and neonatal intensive care unit (NICU). Screening infants at risk and managing hypoglycemia in the first hours and days of life are common challenges in neonatal care. However, its definition, clinical significance and management remain controversial. Current screening guidelines and management algorithms are based on limited evidence and rely more on expert judgement to make recommendations. Studying the incidence may help to plan the services, identifying the clinical features and risk factors associated with neonatal hypoglycemia, may help in preventing neurological damage.

In advent of same the present study was planned to assess incidence, pathophysiology, clinical features, risk factors and management of neonatal hypoglycemia in newborns. Further, the possible outcome of newborn born with neonatal hypoglycemia was also assessed.

MATERIAL & METHODS

After approval from the institutional ethical committee, the present cross-sectional observational study was undertaken between 1st Jan 2021 to 30th June 2022 on 100 neonates born at IMCHRC and admitted at Level III Neonatal Intensive Care Unit, Department of Paediatrics, Index Medical College Hospital & Research Centre, Indore with risk factors for developing hypoglycemia. They were selected randomly at any gestational age after fulfilling the inclusion and exclusion criteria. They were further categorized into males, females, term, pre-term, post-term, appropriate for gestational age, small for gestational age and large for gestational age. A written informed consent was taken from parents/guardians of the study participants.

Inclusion Criteria:

- Pre-term (Small-for-gestational age, Appropriate-for-gestational age, Large for-gestational age)
- Term (Small-for-gestational age, Appropriate-for-gestational age, Large-for gestational age)
- Post-term (Small-for-gestational age, Appropriate-for-gestational age, Large for-gestational age)
- Infant of diabetic mothers (IDM) - insulin dependent and

gestational diabetes
- APGAR >7/10 at 1 minute

Exclusion Criteria
- Babies who were born outside Index Medical College.
- Any baby on IV dextrose as IV fluid within 3 hours of birth
- Patients who did not consented for the study.

METHOD
Blood sugar was screened by glucometer at 1 ,2, 6,12, 24 and 48 hours of age, or whenever any symptoms suggestive of hypoglycemia develops. Detailed clinical history, examinations and necessary laboratory investigations to diagnose hypoglycemia and its associated risk factors in neonates were recorded. For the study purpose hypoglycemia was defined as RBS <45 mg/dl. Blood sugar was screened by glucometer.

Statistical Analysis Plan
The data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was used to prepare the tables. Quantitative variables were expressed as the mean and standard deviation. Categorical data was expressed as percentage. PRISM and Microsoft office was used to prepare the graphs. Student t-test and ANOVA was used to compare the means. Chi Square tut was used to compare the categorical data. P value of < 0.05 is considered as significant.

RESULTS
In present study, 1020 newborns delivered at NICU over a period of 18 months out of 100 newborns enrolled in the study, 36 newborns developed hypoglycemia (36%). Overall incidence is 3.6 per 1000 live births. A higher male preponderance was seen with 59 males & 41 females. Term neonates were 60% whereas 32% were Pre-term and 8% were post term neonates. Majority of the neonates were appropriate for gestational age (70%), 23% were small for gestational age and 7% were large for gestational age. 67% of the neonates were delivered via LSCS whereas 33% were delivered vaginally.The incidence of neonatal hypoglycemia was 36% among NICU admissions. Out of 36 hypoglycemic newborns 16 were symptomatic (45%) and 20 newborns were asymptomatic (55%). This was found statistically insignificant in our study (P<0.05). Out of 36 hypoglycemic newborns majority (56%) of newborns were males whereas females were 44% under the symptomatic group. Among the asymptomatic group 55% were male and 45% were females.

Pre-term neonates were more prone to develop hypoglycemia in both symptomatic and asymptomatic groups (P>0.05). Majority of hypoglycemic newborns were Small for gestational age and birthweight was <2 kg (P>0.05). Term neonates developed hypoglycemia mostly by 6 hours of life. This was found statistically significant in our study (P>0.05).

Pre-term neonates developed hypoglycemia much earlier. Pre-term neonates had more instances of recurrent/persistent hypoglycemia(P>0.05). Jitteriness is a major symptom followed by lethargy that should be thoroughly assessed as an important symptom for hypoglycemia.

Pre-eclampsia is a major maternal risk factor along with gestational diabetes mellitus, leaking per vaginum/bleeding per vaginum and oligohydramnios that can cause hypoglycemia in newborn. These finding were statistically significant (P>0.05).

Prematurity is a major factor followed by respiratory distress that causes hypoglycemia in high-risk neonates (P>0.05). 4 newborns succumbed to death out of which 2 newborns were Male (2%) and 2 newborns were Female (2%). Out the diseased newborns 3 newborns were Pre-Term and 1 newborn was Term. Majority of the newborns that died during the study had associated comorbidities like early of late onset sepsis, convulsions, feeding difficulties etc. that were also responsible for their poor prognosis.

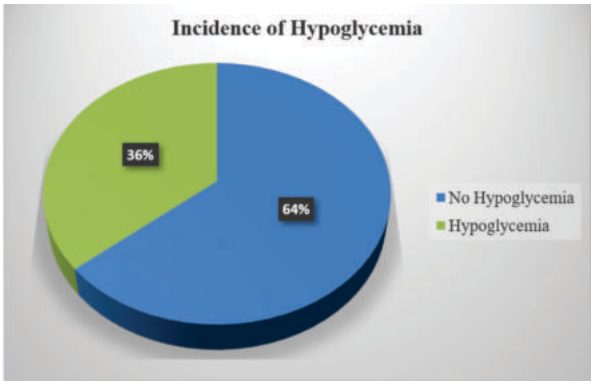

Figure 1. Incidence of hypoglycemia among study population

Table 1. Incidence of hypoglycemia as per the presence of symptoms

	Number	Percentage	P value
Symptomatic	16	45	.650147
Asymptomatic	20	55	
TOTAL	36	100	

Table 2. Gender distribution among newborns with hypoglycemia as per the presence of symptoms

	Symptomatic		Asymptomatic		Total
	No.	%	No.	%	
Male	09	56%	11	55%	20
Female	07	44%	09	45%	16
Total	16		20		

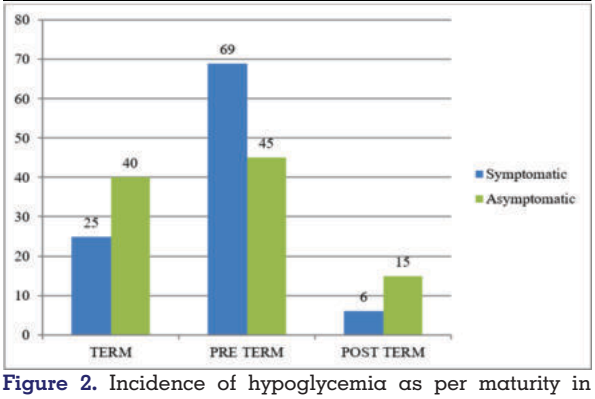

Figure 2. Incidence of hypoglycemia as per maturity in hypoglycemic neonates

Table 3. Maternal risk factors among newborns with hypoglycemia

Diabetes mellitus/GDM	No.	Percentage	P Value
Yes	13	36.2	< 0.00001
No	23	63.8	
Total	36	100	
LPV/BPV	No.	Percentage	
Yes	07	36.2	
No	29	63.8	
Total	36	100	
Thyroid abnormalities	No.	Percentage	
Yes	03	8.3	
No	33	91.7	
Total	36	100	
Oligohydramnios	No.	Percentage	
Yes	06	16.7	
No	30	83.3	
Total	36	100	
Preeclampsia	No.	Percentage	

Yes	15	41.7	
No	21	58.3	
Total	36	100	

Table 4. Fetal risk factors among newborns with hypoglycemia

Septicemia	No.	Percentage	P Value
Yes	12	33.3	< 0.00001
No	24	66.7	
Total	36	100	
Birth asphyxia	**No.**	**Percentage**	
Yes	10	27.8	
No	26	72.2	
Total	36	100	
Prematurity	**No.**	**Percentage**	
Yes	19	52.8	
No	17	47.2	
Total	36	100	
Respiratory distress	**No.**	**Percentage**	
Yes	15	41.7	
No	21	58.3	
Total	36	100	
Neonatal hyperbilirubinemia	**No.**	**Percentage**	
Yes	10	27.8	
No	26	72.3	
Total	36	100	
Polycythemia	**No.**	**Percentage**	
Yes	05	13.9	
No	31	86.1	
Total	36	100	
Meconium aspiration syndrome	**No.**	**Percentage**	
Yes	07	19.4	
No	29	80.6	
Total	36	100	
IUGR	**No.**	**Percentage**	
Yes	06	16.7	
No	30	83.3	
Total	36	100	
Delayed feed	**No.**	**Percentage**	
Yes	10	27.8	
No	26	72.2	
Total	36	100	

Table 5. Distribution of management among newborns with hypoglycemia

Treatment given	Frequency	Percent
Feeding only	22	61%
GIR 6-8	8	22%
GIR 10 and above	6	16%
Total	36	100.0

Table 6. Outcome of newborns among the hypoglycemic newborns and gender distribution

	Survived		Died		Total
	No.	Percentage	No.	Percentage	
Male	57	57%	2	2%	59
Female	39	39%	2	2%	41
					100

DISCUSSION

Neonatal hypoglycemia is common and linked to poorer neurologic outcome. It is a common problem requiring continuous screening and monitoring and often leads to neurological damage if left untreated. The incidence of neonatal hypoglycemia may be increasing as maternal factors known to contribute increase in frequency, including either poor or excessive nutrition, diabetes, increasing maternal age and poor economic conditions. 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.

In present study overall incidence of hypoglycemia among newborns was 3.6 per 1000 live births, whereas 36% among the 100 newborns evaluated. which was higher as compared to studies done by CK **Sasidharan et al**[10] & **Somanathan et al**[11] who reported an incidence of 21% & 14.9% respectively. This can be due to various of reasons. Firstly, the newborns in our study were admitted at level III NICU which is well equipped for management of high-risk newborns. Secondly all babies were screened regularly using a consistent standardized approach and all glucose measurements were analyzed immediately thus increasing accuracy of result.

Out of 36 hypoglcemic newborns, 45% (16) were symptomatic whereas 55% (20) were asymptomatic (P value=0.042858). This shows that nearly 40-50% of newborns become symptomatic and proper assessment of asymptomatic newborns should be done so as to detect early symptoms of hypoglycemia. Results of our study were in accordance with other studies done by **CD Dhananjaya et al**[12], 38 (4.2%) newborn babies were hypoglycemic out of which 60% were asymptomatic and 40% were symptomatic.

Males were more affected than females in our study. No significant reason was found for same This finding is consistent with other studies done by **CD Dhananjaya et al**[12], **& Somanathan et al**[11].

In present study, out of 16 symptomatic newborns with hypoglycemia, 25% were term babies, 69% were Pre-term and 6% were post-term. (p-value is .002059). This is correlating to the fact that pre-term babies have less glucose reserves in the body and are more prone to developing hypoglycemia. This was in concurrence with study done by **CD Dhananjaya et al**[12] In symptomatic groups, majority of hypoglycemic newborns were Small for gestational age (56%) with a statistically significant correlation (P>0.05). This was similar to results of study done by **CD Dhananjaya et al**[12]. The high incidence of hypoglycemia in SGA as well as preterm babies is because of deficient hepatic gluconeogenesis from lipids and amino acids, lack of substrate delivery particularly of lipids to the liver or a combination of the two.

Majority of the newborns belonged to 1000 – 2000 gms weight group (47.2%). Low birth weight babies have higher incidence of developing hypoglycemia. This is in accordance to study by **Saini A et al** [13] in which incidence of hypoglycemia was higher in low-birth-weight babies.

In present study, in term neonates majority of newborns (34%) had at least one symptom of hypoglycaemic episodes by 6 hours of life (P-value = <0.0001) whereas 30% of pre-term newborns had an episode by 2nd hour of life while post-term newborns majority (50%) had an episode by 6 hours of life (50%) Preterm neonates are born with low stores of glycogen and adipose tissues. This situation is further complicated by the fact that several enzymes involved in gluconeogenesis viz. Phosphoenolpyruvate carboxykinase (PEPCK), glucose-6-phosphatase, fructose 1,6-diphosphatase, and Pyruvate caroboxylase are expressed at very low levels limiting their capacity for gluconeogenesis. Preterm infants and those with IUGR are highly likely to become hypoglycemic in the early hours of neonatal period. Preterm neonates had longer duration of hospital stay and are mostly nill by mouth in initial days of birth which makes them more prone for hypoglycemia. This is in accordance with Study by **Deborah et al** [14], **CK Sasidharan et al**[10] **& CD Dhananjaya et al**[12].

Further, majority of the pre-term newborns had recurrent episodes of hypoglycemia & majority were Small of gestational age (50%). In study by **Deborah et al** [14] 98 newborns (19%) had recurrent episodes of hypoglycemia. Hyperinsulinism, secondary to islet cell hyperplasia, is the most common cause of persistent hypoglycaemia during early infancy.

Among the hypoglycaemic newborns, jitteriness (50%) was

most common symptom followed by lethargy and poor feeding (43.7%), hypothermia, apneic spell (31.25%), convulsions (25%) and cyanosis being the least common symptom to appear (18.75%) (P-value=.018752). The results were similar to studies done by **CK Sasidharan et al**[10], **Somanathan et al**[11], **CD Dhananjaya et al**[12]& **Sikandar et al**[15]**.** In the present study the various symptoms were diagnosed effectively as the study was conducted at level III NICU at a tertiary care centre.

Among the maternal risk factors, pre-eclampsia was found to be major maternal risk factor (41.7%) to develop neonatal hypoglycemia followed by gestational diabetes mellitus and leaking per vaginum/bleeding per vaginum (36.2%) (P-value = <0.00001). Infants who are born to pre-eclamptic mothers have increased risk of developing neonatal hypoglycemia and increased risk of longer hospital stay. Preterm and IUGR deliveries are more common in preeclampsia mothers which further increases risk of developing hypoglycemia due to poor glycogen reserves. Gestational diabetes mellitus is common complication in many pregnancies. When diabetes is undiagnosed during pregnancy or not well managed, it can lead to hypoglycemia in newborns due to glucose passing through placenta, elevating plasma glucose level in foetus and ultimately increasing among of insulin in foetus. This is also in accordance to study by **CD Dhananjaya et al**[12], **CK Sasidharan et al**[10] & **Somanathan et al**[11]

Prematurity was found to be major fetal risk factor among the hypoglycemic newborns (52.8%) followed by respiratory distress syndrome (41.7%), septicaemia (33.3%), birth asphyxia, neonatal hyperbilirubinemia and delayed feeding (27.8%), meconium aspiration (19.4%), IUGR (16.7%) and polycythemia being the least common (13.9%) (P-value = <0.00001). Preterm, small for gestational age (GA) and intra uterine growth restricted neonates are especially vulnerable due to their lack of metabolic reserves and associated co-morbidities. Because of their low-calorie intake, higher metabolic rate, slowed rate of gluconeogenesis, and potential for greater peripheral use because of improved insulin sensitivity, neonates with septicaemia are more likely to develop hypoglycemia. Birth asphyxia and perinatal stress increase the risk of hyperinsulinism in the neonatal period because of the use of anaerobic metabolism to maintain blood glucose concentrations. The results were in concurrence with studies done by **CD Dhananjaya et al**[12], **CK Sasidharan et al**[10] & **Sikandar et al**[15] who stated that birth asphyxia had highest incidence of hypoglycemia. In a study done by **Somanathan et al**[11], prematurity had the highest incidence (29%) followed by septicaemia (8.6%), birth asphyxia (5.4%).

In present study, in about 61% newborns neonatal hypoglycemia was corrected by adequate feeding only, around 22% required iv dextrose with glucose infusion rate (GIR) around 6 – 8 mcg/kg/min. Around 16% of newborns required GIR of 10 or above. In study by **Somanathan et al**[11], 72.3% hypoglycemic neonates were corrected by oral feeds. 27.3% required i.v. dextrose and only 0.5% required hydrocortisone. Results were varied from the study done by **Singh et al**[16] which showed 34% hypoglycemia required oral feeds and 66% required i.v. fluids. This shows that if we do proper monitoring of hypoglycemia, majority of the newborns will recover though adequate feeding practices and will decrease chances of giving invasive treatment.

In present study, out of 36 hypoglycemic newborns, only 4 newborns succumbed to death out of which 2 newborns were Male (2%) and 2 newborns were Female (2%). Out the diseased newborns 3 newborns were Pre-Term and 1 newborn was Term. The term newborn that died was infant of diabetic mother with septicaemia. This shows that pre-term neonates are more prone for neonatal morbidity if hypoglycemia is not managed adequately. Overall survival was 96%.

In study by **CD Dhananjaya et al**[12]et al 4 babies died; 3 babies were associated with hypoglycemia. Among 3 cases 2 were preterm and 1 term.

CONCLUSIONS

The incidence of neonatal hypoglycemia was 36% among the 100 newborns evaluated among NICU admissions. The maternal risk factors associated with neonatal hypoglycemia were Preeclampsia, GDM, PIH, PROM and the neonatal risk factors were prematurity, SGA, LGA and comorbid conditions which include perinatal asphyxia, sepsis, polycythemia, shock. Most of the neonates with hypoglycemia were asymptomatic. Among the symptomatic neonates poor feeding was the most common symptom on presentation and most of them achieved euglycemia with oral feeds.

Recommendations

Most of the neonates had risk factor and many of the neonates were asymptomatic, hence mandatory blood glucose screening in neonates at regular interval for blood glucose level more specifically at first 24 hours of life serves as an effective measure for identification for hypoglycemia. Most cases became euglycemic only with oral feeds. Hence focused counselling on the early initiation of breast feeding will reduce the incidence of hypoglycemia and its complications.

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