This study done at AIMS(Belur) when I was doing my PGr.

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Original Article

Clinical profile of hypoglycemia in newborn babies in a rural hospital setting

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ABSTRACT

Objectives : To study the frequency of hypoglycemia, clinical features and the risk factors associated with development of hypoglycemia in newborns. Design: Cross-sectional study Setting:.All babies admitted to NICU, S AH & RC were included in the study. Subjects:. 366 newborn babies admitted to NICU were included in the study during the study period of 18 months. Methods:. Blood sugar was screened by glucometer at 3,24,48 and 72 hours of age or whenever any symptoms suggestive of hypoglycemia develops. Detailed clinical history , examinations and necessary laboratory investigations to diagnose high risk neonates were recorded. Results: 38 Newborn babies were hypoglycemic out of which 60% were asymptomatic and 40% were symptomatic. Males were 22(57.89%), Females were 16(42.10%), overall incidence of hypoglycemia is 4.2%, in that, Preterm -11.9%, Term -2.9% ,SGA-14.75%, LGA-22.22%. 21 cases (55.26%) presented hypoglycemia on day 2, 10 (26.31%) on day 1 and 3 7(18.42%) on day 3. Maternal risk factors contributed to the development of hypoglycemia were IGDM/IDM (40%), prolonged labour (15.35%) and eclampsia (40%). In newborn risk factors causing hypoglycemia, birth asphyxia had highest incidence of 26.86% followed by RDS and septicemia both 15%. In birth asphyxia, term babies were more prone to hypoglycemia with incidence of 61.11%.

1. Introduction

Hypoglycemia is the most common metabolic problem occurring in newborns. In majority of cases, it merely reflects a normal process of adaptation to extra uterine life. The term "hypoglycemia" refers to a reduction in the glucose concentration of the circulating blood. It is almost 100 years since hypoglycemia was first described in children and over 50 years since it was recognized in newborns and infants[1].

"Hypoglycemia is not a medical condition in itself, but a feature of illness or of failure to adopt from the fetal state of continuous transplacental glucose consumption to the extra uterine pattern of intermittent nutrient supply". Variable incidence has been reported by various authors in different weight and gestational age groups[2]. The overall incidence of hypoglycemia in neonates varies from 0.2 to 11.4%. However in the presence of certain risk factors i.e. small for date, large for date, infants of diabetic mothers, prematurity etc., the probability of hypoglycemia increases many folds[3,4].

Hypoglycemia in neonates can be symptomatic and asymptomatic. The most common symptoms such as jitteriness, convulsions, apathy, hypotonia, coma, refusal to feed, cyanosis, high pitched cry, hypothermia are very nonspecific and especially in small sick infants, these symptoms may be easily missed. Therefore hypoglycemia must always be confirmed biochemically and by response to treatment [5, 6, 7]. Hypoglycemia is known to be associated with brain dysfunction and neuromotor developmental retardation in both symptomatic and asymptomatic cases[1, 3, 8].

The glucose infusion varying from 6 to 12mg/kg/min or even higher has be recommended to maintain the desired blood sugar level [9,10,11].Therefore if the glucose requirement in each high risk category is individualized it will help in achieving a stable blood sugar level earlier. The present study was planned to document the clinical profile of hypoglycemia and assess the

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amount of glucose (mg/kg/min) needed in various high risk categories of hypoglycemia babies to achieve a stable blood sugar.

2. Materials and Methods

All neonates born normally or delivered by cesarean section and instrumentation in Sri Adhichunchanagiri Hospital and Research Center, rural tertiary care hospital attached to Adhichunchanagiri Institute of Medical Sciences, Bellur, Karnataka, between November 2004 to April 2006 were included in the study.

For the study purpose hypoglycemia was defined as RBS <40mg/dl. Blood sugar was screened by glucometer at 3,24,48 and 72 hours of age or whenever any symptoms suggestive of hypoglycemia develops.

Detailed clinical history, examinations and necessary laboratory investigations to diagnose high risk neonates will be recorded.Materials used are glucometer(one touch ultra by johnson & johnson 2004), blood glucose strips lancet,dry cotton/spirit swab/sterile swab.

2.1. Glucometer

2.1.1. Test Principle:

Bioamperometry—glucose dehydrogenase in the strip converts the glucose in the blood sample to gluconolactone. This reaction creates a harmless electrical current that the glucometer interprets for that blood glucose.

2.1.2.Procedure

Touch the drop of the blood collected, to the curve at the edge of the test strip. No part of the yellow color on the strip should be visible after applying the initial drop of blood. Blood will be drawn into the strip automatically. Do not place the blood drop on the top of the strip. Test result will appear within 30 seconds.

2.2.Statistical Methods:

Chi-square and Fisher exact test have been used to test the significance of study incidence of hypoglycemia. Odds Ratio has been used to find the strength of relationship between incidence of hypoglycemia and the birth weight and the gestational age.

3. Results

The study was conducted from November 2004 to April 2006 at pediatric department of Sri Adhichunchanagiri Hospital and Research Center is a rural tertiary care hospital attached to Adhichunchanagiri Institute of Medical Sciences, Bellur, Karnataka.

900 babies were born in the hospital during this period. Out of 900, 366 babies were admitted to Neonatal Intensive Care Unit(NICU).

38 Newborn babies were hypoglycemic out of 60% were asymptomatic and 40% were symptomatic.

22 newborn were male babies and 16 newborn were female babies which accounted for 57.89% and 42.1 %respectively.

The overall incidence of hypoglycemia is 4.2%, in that, Preterm - 11.9%,

Term -2.9%
SGA-14.75%
LGA-22.22%

Among the preterm babies, the incidences of hypoglycemia were highest in preterm with SGA (small for gestational age) with the percentage of 25 and lowest in AGA infants.

Among the term babies, the incidence of hypoglycemia was more among LGA (large for gestational age) babies which accounted for 23.07% of cases.

Among the post term, the incidence was more in post term with AGA (appropriate for gestational age) babies with 50% (Table.1)

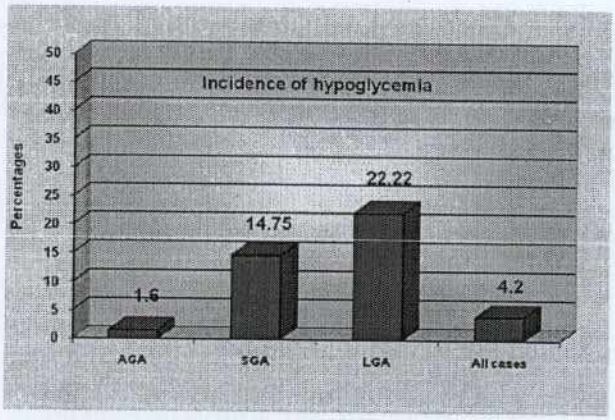
Table 1: Incidence of Hypoglycemia according to Gestational age and birth weight.

	Preterm			Term			Postterm			Total		
	No. of Cases	HYP	PERC	NO. OF CASES	HYP	PERC	NO. OF CASES	HYP	PERC	NO. OF CASES	HYP	PERC
AGA	66	6	9.09%	674	5	7.4%	2	1	50%	742	12	1.6%
SGA	8	2	25%	103	13	12.6%	11	3	27.2%	122	18	14.75%
LGA	10	2	20%	26	6	23.07%	0	0	0%	36	8	22.22%
TOTAL	84	10	11.9%	803	24	2.9%	13	4	30.7%	900	38	4.2%

Inference Incidence of Hypoglycemia in SGA babies is 6.55 times significantly more likely with 2=38.710, P<0.001** And LGA babies are 7.94 times more likely to have hypoglycemia with P<0.001**

Taking all preterm, term and post term babies together the incidence of hypoglycemia was more in large for date babies 22.22%. The overall incidence of hypoglycemia was 4.2% in the present study (Figure.1)

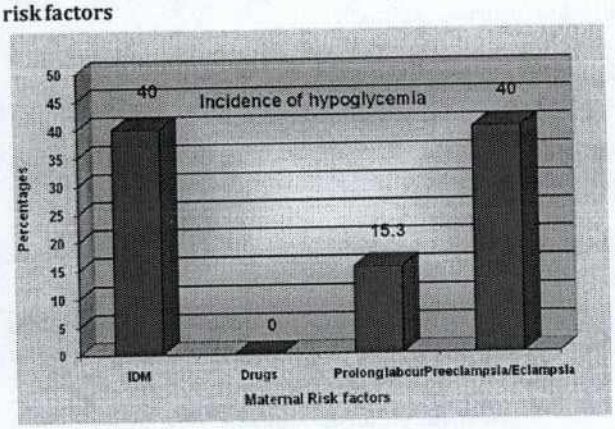
Figure 1: Showing the incidence of hypoglycemia according to Birth weight



In the present study 21 cases (55.26%) presented hypoglycemia on day 2, 10 cases (26.31%) on day 1 and 37 cases(18.42%) on day 3.

In Maternal risk factors the development of hypoglycemia in babies born to mother with gestational diabetes and diabetes mellitus were (40%), prolonged labour (15.35%) and eclampsia (40%)(Table.2)(Figure.2)

Figure 2: Incidence of hypoglycemia in relation to maternal risk factors



In Maternal risk factors the development of hypoglycemia in babies born to mother with gestational diabetes and diabetes mellitus were (40%), prolonged labour (15.35%) and eclampsia (40%)(Table.2)(Figure.2)

Table 2: Incidence of Hypoglycemia in relation to maternal risk factors

Maternal Risk Factors	No. Of Cases	Hypoglycemia (n=38)	Percentage
IGDM/IDM	5	2	40%
Drugs	0	0	0%
Prolong Labour	13	2	15.3%
Preeclampsia/Eclampsia	10	4	40%

Mode of delivery didn't have any significant role in the causation of hypoglycemia in the newborn.

In newborn risk factors causing hypoglycemia, birth asphyxia had highest incidence of 26.86% followed by Respiratory distress syndrome and septicemia both 15% (Table.3)(Figure.3). In birth asphyxia, term babies were more prone to hypoglycemia with incidence of 61.11%.

Figure 3: Incidence of Hypoglycemia in relation to New born risk factors

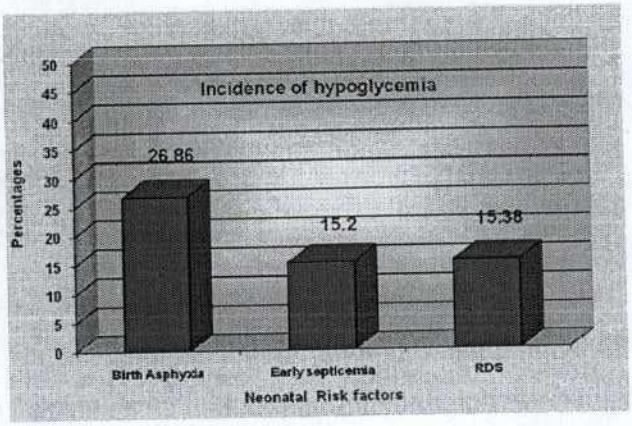


Table 3: Incidence of Hypoglycemia in relation to New born risk factors(n=38)

New Born Risk Factors	No. Of Cases	Hypoglycemia	Percentage
BIRTH ASPHYXIA	67	18	26.86%
EARLY SEPTICEMIA	46	7	15.2%
RDS	13	2	15.38%

In the present study 16 cases had clinical manifestation of hypoglycemia, lethargy(81.25%)and jitteriness(75%) were the most common manifestation followed by respiratory abnormalities (37.5%)., seizures (31.25%) and cyanosis (18.75%) (Table.4)(Figure.4).

Figure 4: Incidence of Hypoglycemia in relation to Clinical features

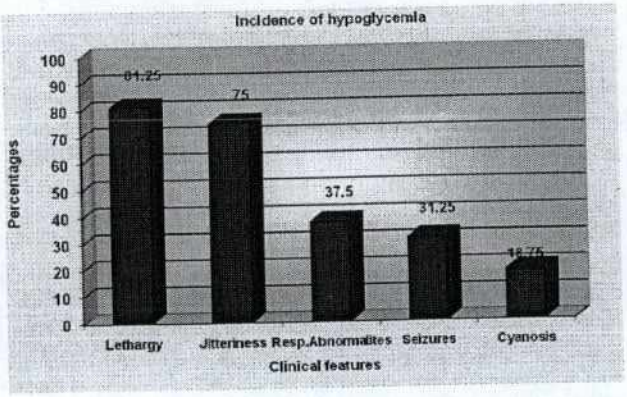


Table 4: Incidence of Hypoglycemia in relation to Clinical features

Clinical Features (n=16)	No. Of Cases	Percentage
Lethargy	13	81.25%
Jitteriness	12	75.00%
Respiratory Abnormalities	6	37.50%
Seizures	5	31.25%
Circumoral Cyanosis	3	18.75%

In the present study, 4 babies died, 3 babies were associated with hypoglycemia. Among 3 cases 2 were preterm and 1 term. Both the preterm cases had early onset septicemia and one of the preterm case had birth asphyxia. The term baby which died in the present study had septicemia and birth asphyxia.

4. Discussion

It is almost a century since hypoglycemia was first described in children and over 50 years since it was first described in newborns. Given the numerous advances which have since occurred in the care of the newborns it is surprising that so much controversy still

surrounds the definition, significance, detection and management of neonatal hypoglycemia. Paradoxically, technological developments in the form of bedside glucose monitoring have exacerbated rather than eased the problem by facilitating screening for an ill-characterized clinical entity [1-5].

The vulnerability of premature infants and those of diabetic mothers, to hypoglycemia was recognized early in the history of neonatal medicine1. The transient nature of hypoglycemia and the apparent infrequency of clinical manifestations led many to assume that low blood glucose concentrations among these groups were innocuous and physiological, in contrast to the hypoglycemia caused by metabolic and endocrine disorders. However, in 1959 Cornblath et al described, two days old infants born to mothers with pre-eclamptic toxemia in whom symptoms [apnea, cyanosis, coma, convulsions] were associated with reduced blood glucose concentrations. They described a clinical response to the infusion of intravenous glucose and drew attention to the "self limited but refractory' course of hypoglycemia. The outcome of this small group of infants was poor12. Further descriptions of the neurological sequelae associated with symptomatic hypoglycemia in the newborn period followed.Concern arouse that hypoglycemia without clinical signs might also lead to neurodevelopmental sequelae [1,9]. This led to an attempt to define hypoglycemia statistically as a blood glucose concentration more than 2S.D below the mean for populations of well full-term and low birth infants1. Estimating the exact frequency of hypoglycemia begs the question of numerical definition. Various studies have recorded a wide varied incidence of hypoglycemia in their studies depending upon the numerical definition used. Long term neurological sequelae were in up to 35% of those with symptomatic hypoglycemia and 20% of those with asymptomatic hypoglycemia [1,12].

In the present study 900 babies were screened for hypoglycemia out of which 38 babies were hypoglycemic.

In the present study the overall incidence of hypoglycemia was 4.2% which was comparable to the P.K.Singhal et al[12] study. Other studies showed slight higher incidence.

In present study, 55.26% of the neonates were found to be hypoglycemic on day 2.

The incidence of hypoglycemia was 26.31% on the 1st day, 55.26% on the 2nd day and 18.42% on the 3rd day. In a study done by M.A.Bhat et al[13] in SGA babies, 98% of the episodes of hypoglycemia occurred within first 24 hours. According to Hawdon et al[14] study on preterm infants the mean blood glucose concentration was significantly lower on the 1st day than on subsequent days.

In Tanzer F et al[15] study (in full term neonates) , lowest blood glucose level was seen in the first 3 hours of life.

In the present study, the incidence of hypoglycemia was found to be more in LGA and least in term babies. The present study incidence correlates well with P.K.Singhal[12]et al study.

The other studies showed a higher incidence of hypoglycemia in preterm, term, SGA and LGA.

The high incidence of hypoglycemia in SGA and 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.

The higher incidence of hypoglycemia in LGA is due to IGDM (undiagnosed)/IDM/birth asphyxia.

In the present study, the incidences of hypoglycemia born to mother with IGDM/IDM, eclampisa were almost equal to when compared to other studies.

The present study shows that babies born to mothers with hypertensive disorder and diabetes mellitus disorder have higher incidence of chances of developing hypoglycemia.

Stage 2 prolonged labour can also produce hypoglycemia. More than two third of the neonates with hypoglycemia and one or more newborn risk factors documented by P.K.Singhalet al[12] study.

The association of birth asphyxia and hypoglycemia documented by P.K.Singhal et al[12] has been recognized by the present study because nearly one fourth of the hypoglycemic infants had low APGAR scores at birth. An increase rate of anaerobic glycolysis in combination with an increased rate of glycogenolysis probably predisposes to hypoglycemia.

In the present study, most of the infant (61.11%) with birth asphyxia and hypoglycemia were of term birth which is comparable to the P.K.Singhal et al[12] study in which 71.5% cases were term birth asphyxia with hypoglycemia. This suggests that the glucose released by the stress is rapidly utilized in term infants, while it is poorly utilized in premature infants.

Our observation is comparable to P.K.Singhal et al[12] study who reported that 11.6% of septicemia cases developed hypoglycemia. Septicemia neonates are predisposed to develop hypoglycemia due to inadequate calorie intake, increased metabolic rate, decreased rate of gluconeogenesis and the possibility of increased peripheral utilization due to enhanced insulin sensitivity.

Due to sepsis more utilization of glucose can give rise to hypoglycemia newborns.

In the present study 15.38% RDS developed hypoglycemia when compared to P.K.Singal et al[12] study which showed 8.9%.

In the present study, lethargy and jitteriness were found to be the commonest symptoms which correlated well with P.K.Singhal et al[12] study.

About one fourth of the symptomatic cases experienced seizures which is comparable to P.K.Singhal et al [12]and P.K.Mishra et al[2] studies.

Respiratory abnormalities were associated in more than one third of infants with hypoglycemia which correlates with P.K.Singhal et al[12] study(41.9%) P.K.Mishra et al[2] reported respiratory abnormalities in 26% cases, while Cornblath et al[3] reported respiratory difficulties in 47% cases.

Circumoral Cyanosis was the least common manifestation seen in the present study which is comparable with P.K.Singhal et al[12] study.

Majority of the cases of cyanosis were peripheral due to hypothermia.

5. Conclusion

Hypoglycemia is a common preventable and neglected problem in developing countries. Our study showed that preterm, LGA's, SGA's, preterm, eclampsia, birth asphyxia, respiratory distress, IGDM/IDM's, septicemia and hypothermia are at an increased risk of developing hypoglycemia. More than half of the cases were asymptomatic even though the blood glucose levels showed hypoglycemia.

Hence these categories of neonates deserve an aggressive blood sugar monitoring and management in order to reduce the early infant mortality and neuro developmental sequelae in later life.

Irrespective of the symptomatic and asymptomatic newborns has to be screened for blood glucose level within 72 hours which can prevent hypoglycemia in turn can prevent tissue damage.

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