NEONATAL HYPOGLYCEMIA– CLINICAL PROFILE AND GLUCOSE REQUIREMENTS

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ABSTRACT

A total of 2248 infants born at All India Institute of Medical Sciences Hospital, New Delhi were selectively screened for hypoglycemia over a period of 15 months. Hypoglycemia (blood glucose <30 mg/dl) was diagnosed in 107 cases (4.8%). Preterm babies had three times increased risk (12.8%) as compared to term babies (3.6%). Small-for-dates (SFDs) and large-for-dates (LFDs) infants were at increased risk of manifesting hypoglycemia (7 and 10 times, respectively) as compared to the appropriate-for-dates (AFDs) babies (2.7%). Approximately two-thirds of the hypoglycemic babies (67.3%) had one or more risk factors including birth asphyxia (24.2%), diabetic mothers (23.8%), respiratory distress (13.9%) and septicemia (11.6%). A total of 59.8% cases were asmyptomatic while the rest had one or more symptoms. The most common symptom observed was lethargy (81.4%), followed by jitteriness (67.4%), respiratory abnormalities (41.9%), hypotonia (39.5%) and seizures (30.2%). The amount of glucose (mg/kg/min) needed to maintain a stable blood sugar in various categories of hypoglycemic babies was observed to be in the following decreasing order of amount; symptomatic babies with seizures (Gp IV), IGDM's/IDM's and symptomatic babies with other features (Gp III), SFDs and LFDs (Gp II) and AFDs (Gp I). Such a categorization of hypoglycemic babies will help to treat them more precisely.

Key words: *Hypoglycemia, Glucose requirements, Small for date, Large for date.*

Hypoglycemia is one of the most common metabolic problems encountered in the newborns. It is known to be associated with brain dysfunction and neuromotor developmental retardation. The overall incidence of hypoglycemia in neonates varies from 0.2 to 11.4%(1-4). However, in the presence of certain high risk factors, *i.e.*, small-for-dates (SFDs), large-for-dates (LFDs), infants born to gestational or insulin dependent diabetic mothers (IGDMs/IDMs), prematurity, *etc.* the probability of hypoglycemia increases many folds and moreover there is a greater need for higher glucose supplements to meet the increased requirements of glucose in these babies. Glucose infusion varying from 6 to 12 mg/kg/min or even higher has been recommended to maintain the desired blood sugar level(5-7). 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 amount of glucose (mg/kg/min) needed in various high risk categories of hypoglycemic babies to achieve a stable blood sugar.

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Material and Methods

A total of 2248 neonates born at All India Institute of Medical Sciences Hospital, New Delhi, from January 1, 1987 through March 31, 1988, were selectively screened for hypoglycemia. Hypoglycemia was defined as a whole blood glucose level of less than 30 mg/dl irrespective of gestation(6).

The study population included: (*i*) preterm babies, (*ii*) small-for-dates (<10th percentile) and large-for-dates babies (>90th percentile)(8), (*iii*) infants of gestational or insulin dependent diabetic mothers (IGDMs/IDM's), (*iv*) infants with birth asphyxia (Apgar score ≤5 at 1 minute), septicemia and respiratory distress, and (*v*) neonates with symptoms/signs suggestive of hypoglycemia. In these babies, blood sugar was screened by dextrostix (Ames) at 2, 4, 8, 12, 24, 36, 48 and 72 hours of age or whenever any symptom suggestive of hypoglycemia was noted. Dextrostix procedural recommendations were strictly followed in order to ensure accurate results. The glucose values obtained by dextrostix method correlated well with the values obtained from our clinical laboratory. However, any reading in the hypoglycemic range on dextrostix was repeated and then verified by blood glucose estimation on autoanalyser (glucose oxidase method).

A total of 107 cases of hypoglycemia were detected during the period of study. In them, blood sugar estimation was repeated hourly till it became normal and subsequently every 2-4 hourly for the next 48 hours. In stable infants, routine feeding consisted of either expressed breast milk or formula feeds (20 kcal/ml) at 2 hours of age and then every 2 hours. An intravenous infusion of 10% dextrose in water at a rate of 60-80 ml/kg/day was given to infants with birth weight of ≤1,500 g and to those who were considered clinically sick.

All the term healthy appropriate-for-dates babies were transferred to the mother and breast feeding was established within 2 hours of age. In these babies the blood sugar estimation was done only when they developed symptoms suggestive of hypoglycemia.

Antenatal, intranatal and immediate postnatal events were observed and recorded. Additional clinical details documented in cases of hyppoglycemic infants included associated risk factors, gestational age, whether AFD/SFD/LFD, and amount of glucose (mg/kg/min) required to maintain a stable blood sugar. Symptoms were attributed to hypoglycemia only when the onset of symptoms coincided with the finding of low blood glucose value and a favourable response to glucose infusion was noted.

Results

Of 2248 infants born at our hospital, during the study period, 107 (4.8%) babies were diagnosed to have hypoglycemia on selective screening as described above. Preterms, small-for-dates, and large-for-dates babies were more vulnerable to hypoglycemia (*Table I*). The other risk factors associated with hypoglycemia included birth asphyxia (24.2%), IGDMs/IDMs (23.8%), septicemia (11.6%) and respiratory distress syndrome (8.9%). Symptoms were observed in only 43 (40.2%) cases of hypoglycemia (*Table II*). Symptomatic babies required a significantly ($p<0.001$) higher amount of glucose (mg/kg/minute) to maintain a stable blood sugar level as compared to those without symptoms (*Table III*).

TABLE I—*Hypoglycemia in Relation to Growth Status and Gestational Age*

Growth status	Gestational age								
	Preterm			Term			Total		
	No.	HYP*	Inc** (%)	No.	HYP	Inc (%)	No.	HYP	Inc (%)
Appropriate-for gestational age	209	20	9.6	1748	32	1.8	1957	52	2.7
Small-for-gestational age	34	7	20.6	72	11	15.3	106	18	17.0
Large-for-gestational age	46	10	21.7	139	27	19.4	185	37	20.0
Total	289	37	12.8	1959	70	3.6	2248	107	4.8

* HYP = Hypoglycemia; ** Inc = Incidence.

TABLE II—*Clinical Features of Infants with Symptomatic Hypoglycemia (n = 43)*

Clinical features*	Number	%
Lethargy	35	81.4
Jitteriness	29	67.4
Respiratory abnormalities**	18	41.9
Hypotonia	17	39.5
Seizures	13	30.2
Circumoral cyanosis	8	18.6

* Individual clinical features are not mutually exclusive.

** Includes tachypnea and apnea.

TABLE III—*Glucose Requirements in the Various Categories of Babies with Hypoglycemia*

High risk categories	Glucose requirement (mg/kg/min)		
	No. of neonates	Mean	SD
1. Asymptomatic	64	9.2	1.3
(*a*) AFDs*	15	6.1	0.9
(*b*) SFDs*	15	8.1	1.8
(*c*) LFDs*	18	8.3	1.9
(*d*) IGDMs/IDMs*	16	10.4	1.1
2. Symptomatic	43	11.1	0.6
(*e*) with seizures*	13	11.5	0.3
(*f*) with other features*	30	10.4	1.3

* include both preterm and term.

p values: 1 *vs* 2 <0.001; a *vs* b,c, <0.01; a *vs* d <0.001; c *vs* d <0.01; e *vs* f,d <0.01.

Discussion

In the present study, which employed at-risk approach to identify cases of hypoglycemia, the incidence was 4.8% of total births. In our study, the blood sugar was not screened in all the healthy term appropriate-for-dates babies. All these babies behaved normally during their stay in the hospital as well during follow-up in the well baby clinic. Because of the selective screening approach it is quite possible that some infants with asymptomatic hypoglycemia might have been missed. In reports on unselected population, the incidence of neonatal hypoglycemia ranges between 0.2 to 11.4%(1-4). The frequency of hypoglycemia was 12.8% in pre-terms, 17% in

small-for-dates (SFDs), 20% in large-for-dates (LFDs) and 23.8% in IGDMs/IDMs. Lubchenco *et al.*(5) reported 20.3% incidence of hypoglycemia in low birth weight or premature infants. Beard *et al.*(9) found that 14 of 41 premature infants became hypoglycemic if fasted for 48 hours, as did 24 of 41, if fasted for 72 hours. Leeuw *et al.*(7) found 24% incidence of hypoglycemia in SFDs. The high incidence of hypoglycemia in SFDs and premature babies is because of deficient hepatic gluconeogenesis from lipids and aminoacids, lack of substrate delivery particularly of lipids to the liver or a combination of the two(10).

More than two-thirds of the neonates with hypoglycemia had one or more high risk factors as documented by other workers(5-8). The association of birth asphyxia and hypoglycemia documented by Lubchenco and Bard(5) and Beard *et al.*(9) has been reconfirmed by the present study because nearly one-fourth of the hypoglycemic infants had low Apgar scores at birth. An increased rate of anaerobic glycolysis in combination with an increased rate of glycogenolysis probably predisposes to hypoglycemia. In the present series, most of the infants (71.5%) with birth asphyxia and hypoglycemia were of term gestation as documented by Gutberlet *et al.*(3). This suggests that the glucose released by the stress is rapidly utilized in term infants, while it is poorly utilized in premature infants(9). The high incidence of hypoglycemia in IGDM/IDM, as revealed in the present study, is in accordance with observations of Kitzmiller(11) who reported that 30-40% of IDGMs/IDMs babies to be hypoglycemic. Yeng(12) noted hypoglycemia in 35.7% of infants with septicemia. Our observations also substantiated similar association. Septicemic neonates are predisposed to develop hypoglycemia due to inadequate caloric intake, increased metabolic rate, decreased rate of gluconeogenesis and the possibility of increased peripheral utilization due to enhanced insulin sensitivity(13).

In the present series, about one-third of neonates with hypoglycemia had one or more symptoms. Lucas *et al.*(14) observed 50% of hypoglycemic neonates to be symptomatic. Hypoglycemia is known to have protean manifestations and none of the symptoms and signs are pathognomonic. Lethargy and jitteriness were found to be the commonest symptoms in our study. Other workers(1,2,4) have also reported jitteriness to be the commonest manifestation. About one-fourth of the symptomatic cases experienced seizures which is comparable to other studies(1,2). Similarly, respiratory abnormalities were associated in more than one-third of infants with hypoglycemia. Mishra *et al.*(1) reported respiratory abnormalities in 26% cases, while Cornblath(4) reported respiratory difficulties in 47% cases. Other documented symptoms include hypotonia and cyanosis. Hypotonia was not reported in the study by Mishra *et al.*(1) while Cornblath *et al.*(4) reported an incidence of 26% which is lower than the incidence of 39.5% reported by us.

Depending upon the amount of glucose required to achieve a stable blood sugar level, the hypoglycemic babies were categorized into four groups: (*i*) *Group I* (very mild) included asymptomatic AFDs, (*ii*) *Group II* (mild cases)–SFDs and LFD's: requiring a significantly higher amount of glucose as compared to Group I, (*iii*) *Group III* (moderate)–IGDMs/IDMs and symptomatic babies with other features: needing a higher ($p<0.01$) amount of glucose as compared to Groups I and II,

(*iv*) *Group IV* (severe)–symptomatic babies with seizures requiring a significantly higher amount of glucose as compared to the rest of the groups. The identification of these groups is essential as it will help in deciding the rate of dextrose infusion in a particular category of hypoglycemic patients. Thus, the symptomatic babies with seizures should be started with a glucose infusion of as high as 10 mg/kg/min while IDGMs/IDMs and symptomatic babies with other features are likely to do well with 8 mg/kg/min. The policy of starting with a higher glucose concentration in at-risk babies will achieve a stable blood glucose earlier thus decreasing the quantum of insult to the brain. However, further well controlled studies are needed to substantiate our observations.

Our study highlights that preterms, SFDs, LFDs, IGDMs/IDMs, and babies with birth asphyxia, respiratory distress, and septicemia are at an increased risk of developing hypoglycemia. These categories of neonates deserve an aggressive blood sugar monitoring as well as different glucose requirements for managing hypoglycemia.

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