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Assessment of Risk of Hypoglycemia in Normal, Healthy and Exclusively Breast Fed Newborns in First 24 – 48 hrs of Life

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Original Research Article

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Abstract: To assess risk of hypoglycemia in normal, healthy and exclusively breast fed newborns in first 24 – 48 hrs of life. A prospective, longitudinal study conducted on 141 normal healthy, exclusively breast fed newborns. Blood glucose was measured at birth, 2hrs, 6 hrs, 12hrs, 18hrs, 24hrs, 36hrs and 48hrs after delivery. The impact of parity, mode of delivery and intrapartum intake of glucose on blood glucose was analysed. Of 141 newborns, 5 had asymptomatic hypoglycemia who responded to a breast feed or formula feed. Incidence of hypoglycemia was 3.5% among all babies, 33.3% in LGA babies, 33.3% in SGA babies and 2.2% in AGA babies. Mean RBS at the time of hypoglycemia was 36.17± 1.7mg/dl. Mean RBS among hypoglycemic babies at birth was 94±41.9 mg/dl. Mean overall age of presentation of hypoglycemia was 6hrs 20 min. Newborns born to mothers with higher intrapartum intake of glucose had higher blood sugar levels at birth followed by dramatic fall in lower blood sugar levels at subsequent 2 hrs and 6 hrs of life. The fluctuations in the blood sugar values were significantly associated with intrapartum glucose intake by the mothers. There was no statistically significant difference in the occurrence of hypoglycemia based on gestational age, parity and mode of delivery. A normal healthy and exclusively breastfed newborn had a significantly high incidence of asymptomatic hypoglycemia, more so in SGA, LGA and male babies. However parity, gestation and mode of delivery did not influence blood glucose levels.
Keywords: Hypoglycemia, random blood sugar, intrapartum glucose intake.

INTRODUCTION

Hypoglycemia in the newborn period, in isolation or otherwise predisposes to long term neurological damage like disturbances in development and intellectual function, and even spasticity, ataxia and seizure can occur. Even healthy, exclusively breast fed newborns are also prone to developing hypoglycemia, if inadequately fed. Dearth of data displaying incidence of neonatal hypoglycemia among healthy breast fed newborns in developing countries, directed us to conduct this study.

MATERIALS AND METHODS

Study Design

Prospective observational longitudinal study.

Inclusion criteria

All newborns, term or preterm (>34wks) with the birth weight of >1500gms born during the predefined time interval.

Exclusion criteria

1. Preterm newborns (<34wks)
2. Very low birth weight (<1500gms)
3. Sick babies
4. Major Congenital malformation
5. Infant born to diabetic mother
6. If blood glucose remained below 40mg/dl despite additional feeding or infants became symptomatic.

One hundred forty one newborns including both healthy term and preterm (more than 34wks of gestation), AGAs , SGAs and LGAs , weighing between 1.5kg to 4.5kg, were enrolled for study at the time of birth.

Capillary blood was collected by heel prick after proper aseptic measure for screening hypoglycemia by reagent strip method. If the values were low (RBS <40 mg/dl) (2.2 mmol/l), it was defined as hypoglycemia and a venous blood sample was sent for laboratory confirmation by glucose oxidase method in an autoanalyzer. RBS monitoring was scheduled at birth, 2 h, 6 h, 12 h, 18 h, 24 hr, 36 hr and 48 h after delivery which was independent of feeding time.

Unexplained lethargy, jitteriness and seizures, tremor, apnea, poor feeding etc. were considered to be clinical signs of hypoglycemia, if they responded to glucose administration. Infants were considered as asymptomatic if low plasma glucose concentration was not associated with clinical signs.

Oral glucon D of differing strengths was given during labour to mothers who delivered vaginally. Infants found to have hypoglycemia were clinically re-examined, given an additional breast-feed or spoon feed and blood glucose reassessed after 30 min. If blood glucose remained below 40 mg/dl despite additional feeding or infants became symptomatic, they were excluded from the study population. Informed consent was obtained from the parents.

Statistical analysis

Data was presented in the form of statistical Tables and charts. SPSS software version 17 was used. Blood glucose values were expressed in the terms of mean and S.D. Two sample t tests were used for validation of quantitative data. For the comparison of proportions i.e, categorical variables chi square test was used. $P<0.05$ was considered as significant. Statistical analysis was done by the Mann whitneysum test, Fisher's exact test, linear by linear association and ANOVA.

RESULTS

There was no case of symptomatic hypoglycemia. However asymptomatic hypoglycemia was detected in 5(3.5%) babies of the 141 newborns. All these hypoglycemics were males. The distribution of cases enrolled or otherwise are shown in Figure-1.

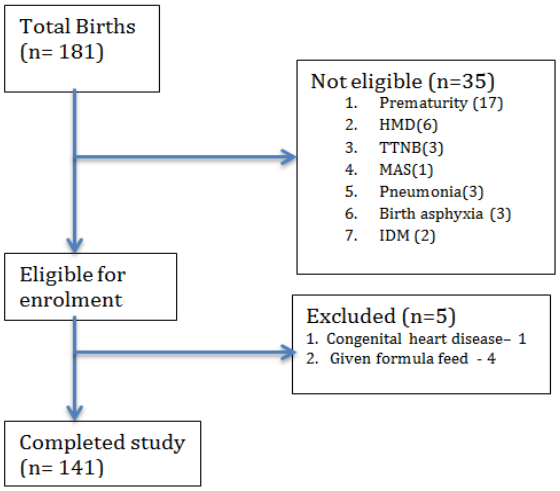

Fig-1: Flow chart for the number of cases

Table-1: Demographics of newborns in the study

Demographic profile	Mean	Range
Mean gestation(wks)	39.40± 1.020 wks	36 – 40 wks
Mean birth weight (grams)	3114± 465.4 gms	1795 – 4690 grams
Mean Apgar score at 1 & 5 min	8.49± .581 , 9.09± .405	7 – 9 & 8 – 10
Male: Female	69:72	
AGA:LGA:SGA	135:3:3	
NBW:LBW	132:9	
LSCS: NVD	77:64	
Preterm: TERM	8:133	
Minor congenital malformations	4	

Table-2: Random blood sugar levels and time of presentation.

Mean RBS levels and age of presentation	Values
Mean RBS at birth of hypoglycemic babies	94 ± 47.9 mg/dl
Mean RBS at birth of hypoglycemic babies	94 ± 47.9 mg/dl
Mean RBS among hypoglycemic babies (during hospital stay)	60 ± 24.2 mg/dl
Mean age of presentation of hypoglycemia (hrs) 1. All babies 2. AGA 3. LGA 4. SGA	 6.20 6.67 2.00 9.00

Mean age of presentation of hypoglycemia was 6.2 hrs among all babies, 6.67 hrs in AGA, 2hrs in LGA and 9 hrs in SGA babies as mentioned in Table-2.

Table-3 reveals maximum fall in blood sugar levels at 2 hrs of life among the total number of babies.

Table-4 reveals maximum fall in blood sugar levels at 6 hours of life in hypoglycemic babies.

Table-3: Blood sugar level distribution according to hours of life(all babies).

Age	Mean (SD)	median	Interquartile range	SEM
Birth	88 ±25.7	84	68 – 106	2.189
2h	68 ±14.3	68	58-76	1.218
6h	67±11.8	69	59 – 75	.996
12h	71±12.1	72	63 – 78	1.023
24h	72±10.5	73	66 – 80	.897
48h	69±10.2	70	64- 78	1.294

Table-4: Blood sugar level distribution according to hours of life in hypoglycemic babies.

Age	Mean (SD)	Median	Interquartile range
Birth	94 ±47.9	73	59 – 139
2h	51 ±17.4	52	35 – 66
6h	48 ±12.5	49	36 – 61
12h	58 ±13.7	64	45 – 68
24h	56 ±8.1	58	48 – 63
48h	62 ±18.9	2	44 – 81

Table-5: Comparison of occurrence of hypoglycemia according to birth weight.

Hypoglycemia	AGA	LGA	SGA
Yes	3	1	1
No	132	2	2
%age	2.2%	33.3%	33.3%
P value	**<.001**		

There was significantly low incidence of hypoglycemia among AGA (2.2%) as compared to LGA (33.3%) and SGA (33.3%) babies , which was even statistically significant (p value <.001) as shown in Table-5.

Though hypoglycemia was seen more among the LBW (11.1%) as compared to normal birth weight (3.0%) babies, it was not statistically significant (p value 0.284).

Although blood sugar levels at the time of birth were in direct correlation with maternal intake of glucose during labour, (p value .000) however, percentage fall in blood sugar levels was highest among those babies whose maternal intake of glucose was highest during labour. e.g, babies of mothers who took 20g/hr of glucose had a fall in mean blood sugar levels from 161mg/dl to 44mg/dl at 6 hrs of life as compared to those babies born to mothers with no intake of glucose during labour, wherein it fell from 74mg/dl to 67mg/dl only at 6 hrs of life.

Table-6: Blood glucose distribution (mg/dl ± SD) according to the intrapartum intake of glucose

Glucose intake	0	5 g/hr	10 g/hr	15 g/hr	20 g/hr	P value
Birth ➔	74±15.3	109±5.8	125±7.6	139±7.0	161±13.4	**.000**
2hrs	66±12.4	75±20.8	71±8.2	56±2.8	90±19.0	**.004**
6hrs	67±11.5	69±13.3	70±8.8	59±9.8	44±12.0	**.035**
12hrs	69±11.5	73±11	79±11.9	70±10.6	53±15.5	**.002**
24hrs	70±10.4	77±9.3	78±9.3	76±.7	66±.70	**.002**
48hrs	69±10.8	73±6.0	69±.7	74± .7	76±12.7	.843

Table-7: Incidence of hypoglycemia according to sex of the baby

Hypoglycemia	male	female
Yes	5	0
No	69	72
%age	**7.2%**	0%
P value	.026	

All the 5 cases of hypoglycemia affected were males which was statistically significant (pvalue .026) as shown in Table-7.

Parity was shown to have an inconsistent effect on hypoglycemic status of babies. (p value- 0.225) as seen in Table-8.

1 out of 8 preterm babies had hypoglycemia whereas in term babies 4 had hypoglycemia out of 133 (p value .257) as depicted in Table-9.

Table-10 reveals an insignificant increase in hypoglycemia amongst babies born by LSCS viz a viz normal vaginal delivery.

Table-8: Incidence of hypoglycemia according to parity of mother

Hypoglycemia	G1	G2	G3	G4
Yes	2	1	2	0
No	79	36	14	7
Total	81	37	16	7
%age	2.5%	2.7%	12.5%	0%
P value	.225			

Table-9: Comparison of occurrence of hypoglycemia according to gestational age

Hypoglycemia	34 – 36+5 wks	37 - 40 wks
Yes	1	4
No	7	129
%age	12.5%	3.0%
P value	.257	

Table-10: Incidence of hypoglycemia according to mode of delivery

Hypoglycemia	NVD	LSCS
Yes	1	4
No	63	73
%age	1.6%	**5.2%**
P value	.377	

DISCUSSION

We observed that the incidence of hypoglycemia was 3.5% among healthy, exclusively breast fed newborns**.** Similar results were shown by Hoseth *et al*., [1] (4%), Hawdon *et al*., [2] (3.4%) and Cornblath *et al*., [3] (5%) while an Indian study by Singhal PK *et al*., [4] at AIIMS, New Delhi showed an incidence of 4.8%. Anderson *et al*., [11] conducted a study wherein incidence of hypoglycemia was 38%. It may be due to higher cut off value of hypoglycemia (2.6mmol/l) in his study. Our comparatively low incidence could be attributed to initiation of early breast feeding within the first hour and low cut off value (2.2mmol/l).

Our study showed that there was significant variation in the blood glucose levels from birth to 2 hours of life. Mean blood sugar level at birth was 88$\pm$25.7 mg/dl and at 2hrs was 68 $\pm$14.3 mg/dl. A similar observation was made by Hoseth *et al.*, [1] in breast fed infants.

Mean RBS at the time of diagnosis of hypoglycemia was 36.17 $\pm$1.7 mg/dl (Range – 33 – 38) in our study. In contrast, Sexson *et al.*, [5] showed lower values of blood sugar at the time of hypoglycemia.

Like the previous observations in cross sectional studies by Hoseth *et al*., [1] and Singhal PK *et al*., [4], we also observed lower sugar levels in the first 24 hours of life. During fetal life, glucose passively diffuses across the placenta, though insulin does not cross the placenta; therefore, the fetus must secrete insulin independently. With the clamping of the umbilical cord, the newborn's supply of glucose ceases while insulin secretion continues. The residual fetal insulin leads to a rapid decline in plasma glucose within the first 24 hours of life.

Mean age of presentation of hypoglycemia in our study was 6 hours 20 min, which was similar to studies by Hoseth *et al*., [1] Bhat *et al*., [6], De AK *et al*., [7] in the breast fed infants. However, amongst LGA babies, hypoglycemia was detected at mean age of 2 hours and in SGA babies at 9.0 hours. This can be explained by transient hyperinsulinemic state in LGA babies, thereby leading to early presentation of hypoglycemia.

In our study the mean blood sugar levels were similar in preterm (71 $\pm$ 17.1 mg/dl) and in term babies (72 $\pm$ 15.9 mg/dl) (p value -.873) but hypoglycemia was noted more among preterm (12.5%) newborns as compared to term newborns (3%) (p value - .257). Similar findings were reported by Hoseth *et al*., [1],

Hawdon *et al*., [2] and Singhal *et al*., [4] who showed a three fold increased risk. Higher incidence of hypoglycemia in preterm babies is probably due to low glycogen stores, immaturity of the glycogenolytic and gluconeogenetic pathways.

In the present study, significantly lower mean blood glucose values and higher incidence of hypoglycemia was found in SGA and LGA than the AGA babies. Incidence of hypoglycemia in AGA, LGA & SGA babies in the present study was 2.2 %, 33.3% & 33.3% respectively (p value <.001). Singhal PK *et al*., [4] showed that SGA and LGA infants were at increased risk of manifesting hypoglycemia (7 and 10 times, respectively) as compared to the AGA babies. SGA infants have fewer glycogen and fat stores than full term neonates attributing to hypoglycemia. However despite low values of blood sugar in LGAs noted in our study and previous studies, no consensus exists among doctors regarding benefits of testing LGAs born to non diabetic mothers for hypoglycemia on routine basis.

Mean blood glucose levels at birth in babies born by LSCS was 79.04 $\pm$21.80 mg/dl and in those born by VD was 99 $\pm$ 25.9 mg/dl (p value <0.001) in our study, which could be correlated with oral intake of glucon D by mother in intrapartum period during trial of normal vaginal delivery.

Infants with the maternal intrapartum glucose intake of 20g/hr continued to have lower blood sugar levels for longer duration upto 12 hrs of life, which was statistically significant. Singhi *et al*., [8] and Lucas *et al*., [9] showed similar results. This situation is akin to that seen in infant of diabetic mothers who also develop transient hyperinsulinemia in response to maternal high blood sugar levels.

Those babies who had low plasma glucose had an immediate restoration to normalcy following a breast feed. Similar results were shown by Diwakar *et al*., [10] who conducted a observational, longitudinal study of healthy exclusively breast fed infants.This could be explained by an adaptive mechanism of glucose homeostasis in breast fed infants. This also explains the increased frequency of feeding seen in exclusively breast fed infants ensures that plasma glucose levels do not remain low for prolonged periods. The ability of the neonatal brain to use alternative fuels such as ketone bodies or lactate for oxidative metabolism may ensure that the infant is symptom free during these transient periods of reduced plasma glucose.

CONCLUSION

A normal healthy and exclusively breastfed newborn had a significantly higher incidence of asymptomatic hypoglycemia while symptomatic hypoglycemia was absent, most likely due to institutional delivery and timely initiation of breast feeds. However there was slightly higher incidence in SGAs, LGAs and male babies . Parity, gestation and mode of delivery had no influence on blood glucose levels. The long term prospective studies to evaluate the effect of lower glucose levels in apparently normal term infants are necessary, before any firm recommendations are made. Hence, it is best to leave the term, breast feeding infant alone rather than treating the biochemical values.

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