
Predictors and Frequency of Convulsions in Neonates with Neonatal Hypoglycemia; a Hospital-Based Study

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Abstract

Introduction: Transient low blood glucose levels are common in neonates as the source of glucose at delivery changes from a continuous supply from the mother to the intermittent supply from feeds. The overall incidence of hypoglycemia has been estimated at 1 to 5 per 1,000 live births, but it is higher in at-risk populations.

Aim of study: To identify predictors, risk factors and frequency of convulsion in hypoglycemic neonates

Patients and methods: A cross sectional study of analytic purpose was performed on 186 hypoglycemic neonates admitted to the neonatal intensive care unit in Maternity Hospital and Raparin Pediatric Teaching Hospitals in the period from February 1st 2010 to June 1st 2011 in Erbil governorate. Neonates presented with symptomatic hypoglycemia and blood glucose less than 30 mg/dl in the first day and less than 40mg/dl after first day were included in the study according to American Academy of Pediatrics criteria of neonatal hypoglycemia. The reading was taken while the neonate was just presented with the symptoms and had not received any glucose solutions.

Results: Overall 4768 neonates admitted to the NICU during the study period; 186(3.9 %) developed hypoglycemia. 111(59.67%) of them were males and 75(40.33%) were female. Convulsions developed in 34(18.27%) of them; out of 34 convulsing hypoglycemic neonates, 20(58%) were males and 14(41%) were females with a male to female ratio of 1.42:1. Low birth weight hypoglycemic neonates more affected with convulsions 25(73.5%) versus normal birth weight neonates 9(26.7%). Premature babies also more affected with convulsions 20(58%) versus appropriate for gestational age babies 14(41.17%).

Conclusions: Neonatal hypoglycemia is a common finding in neonatal care units and may lead to convulsions if not identified early and treated properly, and it's more common in premature, small for gestational ages, infants of diabetic mother and mothers receiving glucose infusions before delivery, while jitteriness, lethargy and apnea were features that most commonly precede neonatal convulsion secondary to hypoglycemia

Key words: neonates, premature, hypoglycemia, convulsions

Introduction

Hypoglycemia is defined as a serum glucose concentration of < 40 mg/dl (< 2.2 mmol/L) in term neonates or < 30 mg/dl (< 1.7 mmol /L) in preterm neonates in the first day of life and less than 50 mg/dl (2.8 mmol/L) after 24 hours of age^[1]. Transient low blood glucose levels are common in neonates as the source of glucose at delivery changes from a continuous supply from the mother to the intermittent supply from feeds^[2].

The overall incidence of hypoglycemia has been estimated at 1 to 5 per 1,000 live births, but it is higher in at-risk populations; for example, it is 8% in large-for-gestational-age infants and 15% in preterm infants and infants who have intrauterine growth retardation^[3].

Glucose is the major energy source for neonate. The newborn brain depends upon glucose almost exclusively. Glucose regulatory mechanisms are sluggish at birth. Thus, the infant is susceptible to hypoglycemia when glucose demands are increased or when exogenous or endogenous glucose supply is limited^[3].

Symptoms of hypoglycemia include apnea, lethargy, inadequate sucking reflex, irritability, irregular respirations, exaggerated moro reflex, cyanosis, pallor, eye rolling, seizures, changes in levels of consciousness, temperature instability, and coma^[4]. Some infants can have documented hypoglycemia but no symptoms^[5].

Hypoglycemia may be due to transient causes like sepsis, asphyxia or hypoxic-ischemic encephalopathy, hypothermia, polycythemia, infant of a gestational or insulin-dependent diabetic

mother, insufficient amount of glucose administration, maternal drugs such as sympathomimetic agents (e.g., propranolol), decreased glycogen stores like Intrauterine growth retardation (IUGR) or small for gestational age, premature infants and postmature infants. Sometimes hypoglycemia is recurrent or persistent either due to hyperinsulinism, hormone deficiencies like Growth hormone deficiency or inborn errors of metabolism^[6, 7].

Patients and methods:

A cross sectional study was performed on 186 hypoglycemic neonates admitted to the neonatal intensive care unit in Maternity and Raparin Pediatric Teaching Hospitals in the period of February 1st 2010 to June 1st 2011 in Erbil governorate.

Neonates presented with symptomatic hypoglycemia and blood glucose less than 30 mg/dl in the first day and less than 40mg/dl after first day were included in the study according to American Academy of Pediatrics criteria of neonatal hypoglycemia^[3]. Neonates with sepsis, meningitis, hypoxia, central nervous system bleeding, metabolic disorders, hypocalcaemia, hypo or hypernatremia were excluded from this study.

Blood glucose level was done for any patient admitted to the neonatal care units. Follow up was done for those neonates suffering from hypoglycemia; blood glucose level was repeated after 1 hour, 2 hours, 6 hours, 12 hours and 24 hours. Perinatal and natal history was obtained about the presence and duration of symptoms like alteration in

level of consciousness, convulsion, onset of and pattern of convulsion, jitteriness, apnea, cyanosis, irritability, prenatal history, maternal diseases, maternal medications taken during pregnancy, intravenous fluids taken before delivery, onset of feeding and family history of convulsions

The reading was taken while the neonate was just presented with the symptoms and had not received any glucose solutions. Hypoglycemia was defined as blood glucose less than 30 mg/dl in the first day and less than 40mg/dl after first day [1].

Statistical analysis was performed with software package "SPSS program version 19" .

The study sample was divided into two groups: Group1 (cases, hypoglycemia with convulsions), Group 2(control, hypoglycemia without convulsions). Chi-square was used as indicated. P value of <0.05 was considered significant.

Results:

Overall 4768 neonates admitted to the NICU during the study period; 186(3.9 %) developed hypoglycemia .111(59.67%) of them were males and 75(40.33%) were females (male to female ratio was1.48:1) .Convulsion developed in 34(18.27%) of them; out of 34 convulsing hypoglycemic neonates, 20(58%) were males and 14(41%) were females with male to female ratio of 1.42:1.

Low birth weight hypoglycemic neonates were more affected with convulsion 25(73.5%) versus normal birth weight neonates 9(26.7%) and this result was highly significant. Premature babies were also more affected with convulsion 20(58%) versus appropriate for gestational age babies 14(41.17%) when the values were statistically significant (p= 0.039) as shown in table -1.

Table- 1: - Characteristics of the study groups in neonatal hypoglycemia

Characters	Characters	Convulsing hypoglycemia Number (%)	Non-Convulsing hypoglycemia Number (%)	P value
Gender	Male	20(58)	81(57.)	0.9
	Female	14(41)	61(43)	
Birth weight	<2.5 kg	25(73.5)	48(33.8)	0.0002
	≥2.5 kg	9(26.7)	94(66.2)	
Gestational age	≥37weeks	14(41.17)	90(63.3)	0.0208
	< 37 weeks	20(58)	52(36.7)	

Concerning full-term neonates who developed convulsions secondary to hypoglycemia; 9(64.28%) were small for gestational age, and the rest 5(35.71%) were appropriate for gestational age

,while most of the premature babies who developed convulsions were low birth weight 16(47.05%), this was statistically significant (P=0.0262,0.0138 respectively) as shown in table 2.

Table- 2: birth weight and gestational age role in hypoglycemic convulsion

Gestational age	Birth weight (kg)	Convulsing hypoglycemia Number (%)	Non-Convulsing hypoglycemia Number (%)	P value
Term	> 2.5	5(14.70)	67(47.18)	0.0137
	≤ 2.5	9(26.47)	27(19.01)	
Preterm	> 2.5	4(11.76)	22(15.49)	0.0277
	≤ 2.5	16(47.05)	21(14.78)	

The highest risk factors which was associated with neonatal convulsion secondary to hypoglycemia was encountered in those mothers who were between 20-35 years old but this was not statistically significant (p= 0.4531), while maternal parity was significant statistically (p= value 0.0202),while those mothers who gave vaginal delivery and who were educated found to be significant statistically (p= 0.0116, 0.02208)

Maternal diabetes mellitus was present in considerable number of mothers especially in those

who developed convulsion, and it was seen to be a considerable risk factor for increasing hypoglycemic convulsion (p= 0.0186).

The babies of mothers who received intravenous glucose water before delivery developed hypoglycemia and convulsion more frequently, and it was a considerable risk factor (p= 0.0062). Further considerable data and relative risk factors with confidence interval of 95% are given in table 3

Table- 3: maternal risk factors of convulsion in neonatal hypoglycemia

Characters	Character	Convulsion with hypoglycemia Number (%)	Non-Convulsion hypoglycemia Number (%)	P value
Maternal age	< 20 years	4 (11.76)	27 (19.01)	0.4531
	20 - 35 years	26 (76.47)	90 (63.38)	
	> 35 years	4 (11.76)	25 (17.60)	
Mode of delivery	Normal vaginal delivery	28 (82.35)	80 (56.33)	0.0116
	Caesarian section	7 (20.58)	62 (43.66)	
Parity	Primigravida	16 (47.07)	36 (25.35)	0.0202
	Multigravida	18 (52.94)	106 (76.64)	
Education status	Educated	21 (61.76)	68 (47.88)	0.02208
	Not educated	13 (38.23)	74 (52.11)	
Residence	Urban	29 (85.29)	121 (85.21)	1
	Rural	5 (14.70)	21 (14.78)	
Diabetes mellitus	Yes	15 (44.11)	33 (23.23)	0.0186
	No	19 (55.88)	109 (76.76)	
Family history of convulsion	Positive	5 (14.70)	7 (4.92)	0.0571
	Negative	29 (85.29)	135 (95.07)	
Socioeconomic status	Low	13 (38.23)	39 (27.46)	0.2176
	Medium and high	21 (61.76)	103 (72.53)	
Intravenous glucose infusion before delivery	Yes	21 (61.76)	50 (35.21)	0.0062
	not	13 (38.23)	92 (64.79)	

Small for gestational age was highly observed as a risk factor for hypoglycemic convulsion which increased the risk by three folds and the difference between studied groups was highly significant (p= 0.0002).

Out of 34 convulsing hypoglycemic neonates, 15(44.11) were infants of diabetic mothers, while out of 142 cases of neonatal hypoglycemia that did

not develop convulsion 33(23.23) were infants of diabetic mothers, and it shown to be a risk factor for developing convulsion secondary to hypoglycemia (p 0.0423). Polycythemia and hypothermia were also considerable risk factors and they were highly significant (P 0.0096). (P= 0.0022) respectively, As shown in table 4

Table- 4: Neonatal risk factors of convulsion hypoglycemia

Characters	Convulsing hypoglycemia No. (%)	Convulsing non-hypoglycemia No. (%)	RR	CI	P value
Small for gestational age	25 (73.52)	49 (34.5)	3.302	1.900 -7.717	0.0002
Infant of diabetic mother	15 (44.11)	33 (23.23)	2.105	1.167 -3.799	0.0186
Polycythemia	13 (23.52)	24 (16.9)	2.326	1.290 - 4.192	0.0096
Hypothermia	7 (20.58)	5 (3.52)	3.543	1.965 - 6.390	0.0022

Concerning types of hypoglycemic convulsions, clonic convulsion was shown to be the most common type, followed by subtle type, and the least

countable type was myoclonic convulsion, as shown in figure 1

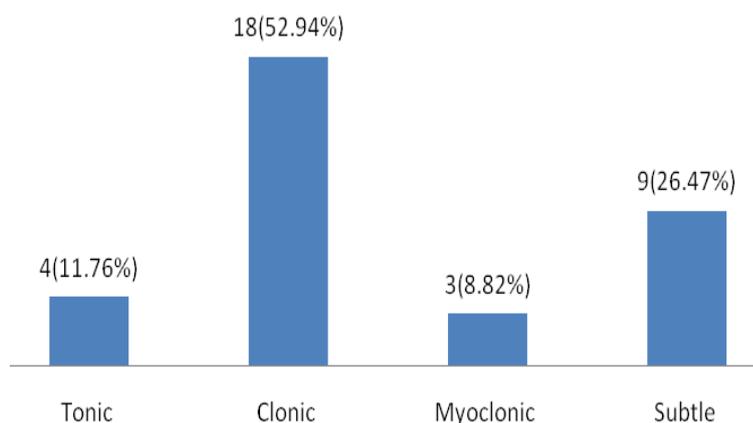


Figure-1: Pattern of convulsions in neonates with hypoglycemia

Most of convulsions occurred in the first day and second day of life, as shown in figure-

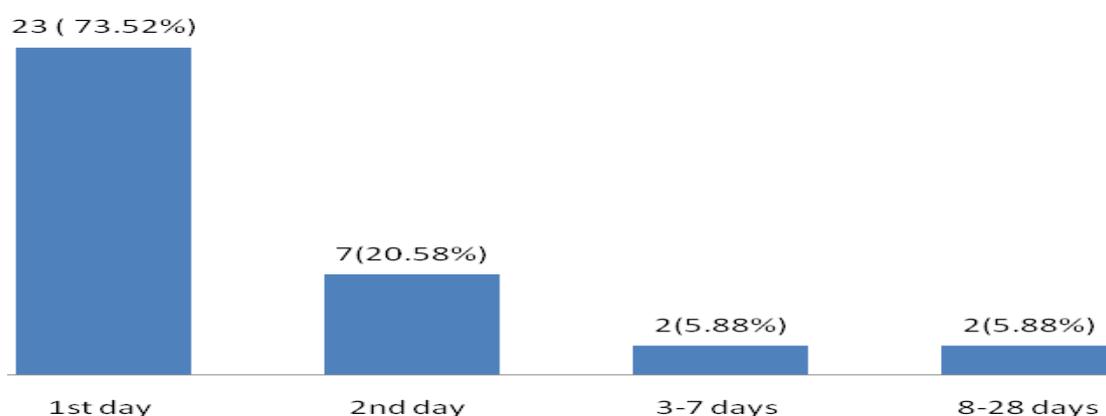


Figure-2: Onset of convulsions in neonates with hypoglycemic convulsion

There were other features associated with neonatal hypoglycemia and led to convulsions, which were compared in both studied groups. Jitteriness was the most encountered associated feature 29(85.29%) cases out of total 34 cases (p 0.023). Furthermore

,presence of apnea was statistically significant association (p 0.0197); while other associated features were not statistically significant, as shown in table- 5.

Table-5: Clinical signs and symptoms in convulsing and non convulsing hypoglycemic neonates

Clinical feature	Status	Convulsing hypoglycemia Number (%)	Non Convulsing hypoglycemia Number (%)	P value
Jitteriness	Present	29 (85.29)	91 (64.09)	0.023
	Absent	5 (14.70)	51 (35.91)	
Poor sucking	Present	25 (73.52)	84 (59.15)	0.1682
	Absent	9 (26.47)	58 (40.85)	
Irritability	Present	14 (41.17)	45 (31.70)	0.3159
	Absent	20 (58.82)	97 (68.3)	
Lethargy	Present	21 (23.52)	55 (38.73)	0.0202
	Absent	13 (76.47)	87 (61.26)	
Apnea	Present	9 (26.47)	14 (9.85)	0.0197
	Absent	25(73.52)	128(90.14)	
Hypotonia	Present	7(20.58)	33(23.23)	0.8234
	Absent	27(79.41)	109(76.76)	
Cyanosis	Present	4(11.76)	21 (14.79)	0.3323
	Absent	30(88.23)	121(85.21)	

Discussion:

In this study the frequency of hypoglycemia appeared to be 186 (3.9%) patients in 4786 admitted cases, this finding agrees with Cornblath M^[1] who found that the overall incidence of neonatal hypoglycemia was 1 to 5 per 1,000 live births, 8% of large-for-gestational-age infants and 15% of preterm infants and neonates presenting with intrauterine growth retardation. The incidence in the entire population of "high-risk" infants may be as high as 30%, these high percentages of hypoglycemia probably because of other associated risk factors of hypoglycemia.

In one study performed on large for gestational age neonates^[8], they found that 16.2% of them developed hypoglycemia and 1.3% of them developed seizures, This value is lower than our findings probably because our study included all neonates admitted to the nursery for observation including premature and small for gestational age neonates.

Low birth weight neonates were more affected with convulsions compared with normal birth weight neonates, this agreed with V Udani et al^[9], they found that hypoglycemia and its complications were more evident in preterm babies (81.2%) versus (18.8%) in term babies as the fetus has continuous glucose supply from intrauterine life and this changes to intermittent glucose supply through feeding and requirement of premature baby to maintain normal glucose level is 5-6 mg/kg/min while term neonates are in need for 3-5 mg/kg/min in contrast to old children who need only 2-3 mg/kg/min, infants delivered prematurely have an abbreviated or no third trimester and thus have limited glycogen stores^[10]; this findings also agrees with Duvanel CB, Fawer C-L, Cotting J, et al^[11] they found that 73% of premature newborns developed hypoglycaemia and this is occurs because the hepatic glycogen stores are limited in both preterm infants, who have not experienced the period of rapid glycogen accumulation during late gestation, and small-for-gestational age infants, who have not had adequate substrate supply available for glycogen synthesis, which puts these newborns at risk for hypoglycemia^[12].

This study found that hypoglycemia led to convulsions in neonates which is probably because glucose turnover is greatest in the premature infant which is because their relatively increased brain-to-body mass ratio that makes them more prone to develop convulsions during hypoglycemia^[13].

Considerable number of neonates who developed convulsion was born from diabetic mothers. This was compatible with Yager JY^[14]; as the infant of diabetic mother has increased secretion of insulin because of increased exposure to high maternal glucose concentration in utero, placental glucose transport is increased leading to fetal hyperglycemia, which in turn stimulates secretion of insulin, by pancreas. After delivery increased glucose secretion no longer persist but hyperinsulinemia persists.

The babies of mothers who received intravenous glucose water before delivery developed hypoglycemia and convulsions more frequently, and it was a considerable risk factor as it expose neonate to high glucose level which stimulate insulin secretion, while after cessation of the intravenous glucose supply blood glucose declines with high insulin level that leads to hypoglycemia this was compatible with Yager JY^[14]. Other data were not compared as there was limited data availability.

Small for gestational age was highly observed as a risk factor for hypoglycemic convulsion which increased the risk by three folds and the difference between both groups was highly significant.

Most of the convulsions (73.52%) occurred in the first week and mainly in the first 72 hours of life, this finding agrees with Rima M Saliba et al^[15] who found 79.8% of convulsions occurred in the first 72 hours and the 52.53% of cases occurred in the first 24 hours.

There were other modes of presentation associated with neonatal hypoglycemia and led to convulsions, which were compared in both studied groups. Jitteriness was the most encountered associated feature 29(85.29%) cases. Furthermore, presence of apnea was also evident remarkable, this findings agree with

Hüseyin Per et al^[16], who found that sucking intolerance in majority of cases of hypoglycemic convulsions; while jitteriness and irritability were the most associated features of neonatal hypoglycemia.

Conclusions:

Neonatal hypoglycemia is a common finding in neonatal care units and may lead to convulsions if not identified early and treated properly, and it's more common in premature, small for gestational ages, infant of diabetic mother and mothers receiving glucose infusions before delivery, while jitteriness, lethargy and apnea were features that most commonly precede neonatal convulsion secondary to hypoglycemia

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