

To Study the Clinico-Etiological Factors of Neonatal Hypoglycaemia

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Abstract

Hypoglycemia in neonates is a common clinical problem and is associated with wide variety of disorders. However, its definition, clinical significance, and management remain controversial. Studying the incidence may help to plan the services, identifying the risk factors associated with hypoglycemia, may help in preventing neurological damage due to neonatal hypoglycemia. *Aims and Objectives:* To study clinical profile of neonatal hypoglycemia. To study the causes responsible for neonatal hypoglycemia. *Materials and Methods:* All neonates admitted in NICU both Inborn and Outborn were included in the study and BSL less than 40 mg/dl was taken as hypoglycemic. *Results:* Fifty seven percent of the babies had hypoglycemia, out of which preterm babies had highest percent of hypoglycemia. Septicemia accounted for 65.3% of the hypoglycemic cases. Lethargy was the most common symptom among hypoglycemia. Home delivery also had significant association with hypoglycemia cases. Among the total death of the hypoglycemic babies, HIE III was the most common cause. Lab values well correlated with glucometer readings. Incidence of hypoglycemia was most during the first 3 hours of life.

Introduction

Hypoglycemia in new born age group is a common clinical problem and is associated with a wide variety of disorders. The neonate is particularly at risk to disequilibrium in carbohydrate metabolism, with hypoglycemia being the commonest clinical problem.

It is established that the persistent early and prolonged hypoglycemia results in brain damage and mental retardation.

Thus, neonatal intensive care therapy units must see all neonates with risk of neonatal hypoglycemia, and to early initiate the treatment, because early recognition offers the best outcomes.¹ Blood glucose concentration in a new born baby irrespective of its birth weight and gestation are generally lower than those found in older children and adults. The

neonate is born with blood glucose concentration of 60-70% of its maternal level and it falls during the first 24 hrs. The lowest value is seen at the age of 3 hrs. This is followed by transient rise in blood glucose level during next 24 hours and again dangerously low level may be encountered at the age of 3-4 days before stability is achieved.

Current recommendations are based in part on statistical analysis in ranges of blood glucose level and poor neurodevelopment outcomes caused by hypoglycemia of neonates with varying blood glucose level. Blood glucose level should be maintained above 40 mg/dl in all neonates of all ages. Further well-suited manifestations relieved by glucose administration at blood glucose level lower than 45 mg/dl should also be considered due to the cause of hypoglycemia.² Hypoglycemia is a common problem in seriously ill or extremely low birthweight infants. If not due to maternal

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hypoglycemia, in most cases it is multifactorial, transient and easily supported. In a minority of cases hypoglycemia turns out to be due to significant hyperinsulinism, hypopituitarism or an inborn error of metabolism and presents more of a management challenge.

Transient neonatal hypoglycemia occurs due to

- (1) Prematurity, intrauterine growth retardation, perinatal asphyxia
- (2) Maternal hyperglycemia due to diabetes or iatrogenic glucose administration
- (3) Sepsis
- (4) Prolonged fasting (e.g., due to inadequate breast milk or condition interfering with feeding)
- (5) Congenital hypopituitarism
- (6) Congenital hyperinsulinism, several types, both transient and persistent
- (7) Inborn errors of carbohydrate metabolism such as glycogen storage disease

The observations suggest that asymptomatic hypoglycemia proceeds less risk of brain damage compared with symptomatic hypoglycemia are limited, as are the observations that associate prolonged hypoglycemia with greater risk of damage than brief hypoglycemia. Limited data available suggests that seizures due to hypoglycemia greatly worsen prognosis. The lack of clear defined data concerning the potentially damaging effects necessitate that all hypoglycemia infants whether symptomatic or not, should be appropriately treated.³

Aims and Objectives

- (1) To study clinical profile of neonatal hypoglycemia.
- (2) To study the causes responsible for neonatal hypoglycemia.

Materials and Methods

All neonates admitted in NICU both Inborn and Outborn were included in the study and BSL less than 40 mg/dl was taken as hypoglycemic study done at a tertiary care hospital over a period of 1 year. Babies admitted to Neonatal intensive care unit with whole blood sugar levels <40 mg/dl were taken up for the study. A written informed consent was taken from either of the parents of the babies. Babies with Congenital malformations, Neonatal

cord injuries, inborn errors of metabolism, maternal history of oral hypoglycemic agents, beta sympathomimetics and maternal glucose infusions during delivery were excluded from the study.

All babies admitted to Neonatal intensive care unit were subjected to Random Blood Glucose estimation initially by strip method using a Glucometer and in babies who show blood sugar levels <40 mg/dl.⁴

Results

A total of 242 cases were admitted to NICU during the study period and 20 cases had hypoglycemia. Neonatal hypoglycemia constituted about 4.13% of our total Neonatal intensive care unit admissions. Majority (60%) of hypoglycemic babies was preterm babies and 40% were term babies. More number of male babies (60%) had hypoglycemia with male to female ratio of 1.35:1. Asymptomatic hypoglycemia was noticed in more number of babies (55%) than symptomatic hypoglycemia (45%).⁵ (Table 1)

Table 1: Clinical Profile

| Characters | Number of cases (n=20) | Percentage (%) |
|--|------------------------|----------------|
| Gestational age | | |
| Term | 8 | 40 |
| Preterm | 12 | 60 |
| Sex | | |
| Male | 12 | 60 |
| Female | 8 | 40 |
| Nature of Hypoglycemia | | |
| Symptomatic | 9 | 45 |
| Asymptomatic | 11 | 55 |
| Symptoms of Hypoglycemia* | | |
| Jitteriness | 11 | 55 |
| Convulsions | 2 | 10 |
| Apneic spells | 2 | 10 |
| Lethargy | 5 | 25 |
| Maternal risk factors† | | |
| Diabetes mellitus | 1 | 5 |
| Ante partum hemorrhage | 2 | 10 |
| Pregnancy induced hypertension (PIH) | 7 | 35 |
| Twin pregnancy | 2 | 10 |
| Neonatal risk factors‡ | | |
| Birth asphyxia | 3 | 15 |
| Intrauterine growth restriction (IUGR) | 7 | 35 |
| Prematurity | 11 | 55 |
| Sepsis | 2 | 10 |

Asymptomatic hypoglycemia was predominantly noticed in preterm babies (55%) than that of term babies. Term babies (45%) showed more symptoms with hypoglycemia than preterm babies.

The major clinical manifestations were jitteriness (55%) followed by lethargy (25%), convulsions (10%) and apneic spells (10%). We noticed PIH (Pregnancy induced hypertension) as the most significant maternal risk factor associated, accounting for 35%. We found prematurity and IUGR the most associated neonatal risk factors for neonatal hypoglycaemia. Significantly low Sugar levels (p value <0.005) were noticed in symptomatic hypoglycemic babies when compared to asymptomatic hypoglycemic babies.⁶ (Table 2)

Table 2: Comparison of mean blood sugar levels with standard deviations between symptomatic and asymptomatic cases

| Number of Cases n = 20 | Mean blood sugar levels (mg/dL) with standard deviations |
|------------------------|--|
| Symptomatic (n = 9) | 26.17 \pm 4.004 mg/dl |
| Asymptomatic (n = 11) | 30.64 \pm 5.113 mg/dl |

Clinical Presentations

- Early transient-adaptive
 - (Asymptomatic transient)
 - Follows withdrawal of substrate from mother
 - LGA (including IDM); preterm asphyxiated/stressed infants
 - Mean age of diagnosis: 3 hours
 - Duration: brief
 - Frequency: 50–75% of cases
 - Classic transient
 - (Symptomatic transient)
 - Associated with poor intrauterine nutrition
 - May be term or preterm; often SGA
 - Mean age of diagnosis: 17 hours
 - 14% will present after 72 hours of age
 - Duration: Prolonged; usually symptomatic (80%)
 - Frequency: 5–25% of cases
- Secondary-Associated
 - Associated with another neonatal problem
 - About half are symptomatic
 - AGA term & preterm; SGA
 - Asphyxia, sepsis, ICH, cold injury, congenital anomalies, CHD
 - Mean age of diagnosis: 16 hours
 - Duration: brief
 - Frequency: 25–50% of cases
 - Severe recurrent
 - (Symptomatic, specific etiology)
 - Term AGA infant with a primary disorder of glucose homeostasis
 - Mean age of diagnosis: 18 hours
 - Duration: Prolonged & recurrent; usually symptomatic
 - Frequency: $<5\%$ of cases.⁹

Discussion

Neonatal hypoglycemia is a common metabolic disease due to inability to maintain glucose homeostasis. The overall prevalence depends on definition of hypoglycemia, criteria for diagnosis of hypoglycemia, diagnostic methods and other factors. Hypoglycemia can present without apparent symptoms, the so called asymptomatic hypoglycemia found in neonates at risk of hypoglycemia.⁷ In our study most babies (55%) had asymptomatic hypoglycemia. Neonatal Hypoglycemia can have variable presentation. In our study jitteriness was accounting for 55%. We noticed convulsions in about 10% of cases; Apneic spells in the present study (10%). Lethargy constituted 25% of cases. There were various maternal risk factors for neonatal hypoglycemia. In present study we found that Pregnancy induced hypertension (PIH) was the most significant risk factor associated with hypoglycemia, accounting for 35% of cases, followed by Antepartum hemorrhage and twin pregnancy. Out of the neonatal risk factors studied in the present study we found that prematurity (60%) was the most significant risk factor followed by intrauterine growth restriction (IUGR) (35%), birth asphyxia (15%), sepsis (10%).⁸

Manifestations

Clinical manifestations that have been attributed to hypoglycemia may be divided as:

1. Activation of ANS
2. Due to cerebral glucopenia
3. Other non specific

Features associated with activations of Autonomic Nervous System and epinephrine release:

1. Anxiety
2. Perspiration
3. Pallor
4. Tremulousness
5. Weakness
6. Hunger
7. Nausea
8. Emesis

Features associated with cerebral glucopenia:

1. Mental confusion
2. Visual disturbances (acuity, diplopia)
3. Organic personality changes
4. Inability to concentrate
5. Staring
6. Paresthesia/Dizziness
7. Amnesia
8. Ataxia, Incoordination
9. Somnolence, Lethargy
10. Seizures
11. Coma
12. Stroke, Hemiplegia, Aphasia
13. Decerebrate or decorticate posture

Non-Specific features:

1. Tremors, jitteriness or irritability
2. Seizures, coma
3. Lethargy, apathy and limpness
4. Poor feeding, vomiting
5. Apnea
6. Weak or high pitched cry
7. Cyanosis

Some infants may have no symptoms.¹⁰

Conclusion

Neonatal hypoglycemia constituted about 4.13% of NICU admissions. Hypoglycemia in neonates can have variable presentations indicating the need for detailed and thorough examination for evidence of hypoglycemia. Identification of risk factors of hypoglycemia and proper monitoring blood glucose levels should be done to plan early treatment and prevent neurological damage.¹¹

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