

Risk Factors and Clinical Features of Neonatal Hypoglycemia: A Prospective Study.

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ABSTRACT

Background: Neonatal hypoglycemia is one of the important causes of morbidity and mortality in neonatal period. It usually presents with lethargy, refusal to feed, hypothermia and seizures. Since in many cases neonates may be completely asymptomatic or may present with subtle manifestations it is important to keep a high index of suspicion for diagnosis of neonatal hypoglycemia. Knowledge about maternal as well as neonatal factors associated with hypoglycemia will help in early diagnosis. **Methods:** This was a prospective observational study conducted in the department of pediatrics of a tertiary care pediatric center situated in an urban area. 60 Neonates admitted in neonatal intensive care unit and found to have symptomatic hypoglycemia at the time of admission or during NICU stay were included in this study on the basis of a predefined inclusion and exclusion criteria. Maternal as well as neonatal factors associated with neonatal hypoglycemia and clinical findings were studied. **Results:** Out of these 60 neonates there were 35 males and 25 females with a M:F ratio of 1:0.71. majority of the cases were having low birth weight (37/60). Normal birth weight (<2.5 kg) was seen in 12 (20%) patients whereas very low birth weight (<1.5 kg) and extremely low birth weight were seen in 7 (11.67%) and 2 (3.33%) patients respectively. Macrosomia (>4kg) was seen in 2 (3.33%) cases. 38 (63.33%) neonates were full term neonates (> 37 weeks) where as preterm (< 37 weeks) were 20 (33.33%). Post maturity (>42 weeks) was seen in 2 cases (3.33%). In 11 (18.33%) cases gestational diabetes was seen in mother whereas pre-eclampsia or eclampsia and Premature rupture of membranes were seen in 6 (10%) and 5 (10%) cases respectively. The most common neonatal risk factor was found to be birth asphyxia (26.67%) and most common presenting complaint was refusal to feed which was seen in all 60 (100%) cases. **Conclusion:** Neonatal hypoglycemia may present with very subtle clinical features. Knowledge about risk factors, maternal as well as neonatal, and presenting complaints is essential for its early diagnosis.

Keywords: Neonatal Hypoglycemia, Refusal to feed, Seizures, Maternal and Neonatal risk factors.

INTRODUCTION

Neonatal Hypoglycemia is one of the important causes of neonatal morbidity and mortality. Although there are many controversies regarding definition of neonatal hypoglycemia, a blood glucose level less than 47 mg/dl is taken by many as diagnostic of neonatal hypoglycemia. It must however be noted that blood glucose level may reach even below 30 mg/dl in neonates 1 hour after birth and this is normal in many healthy term neonates. But this hypoglycemic state is transient and blood glucose level starts rising after this till it gets stabilized over next hours and days of postnatal period. It is therefore because of this reason that many researchers have been reluctant to accept cutoff value of 47 mg/dl as diagnostic of neonatal hypoglycemia.^[1]

The risk factors for neonatal hypoglycemia include prematurity, intrauterine growth restriction,

polycythemia, sepsis, adrenal insufficiency, birth asphyxia and inadequate feeding. In Indian setup and in many other developing countries improper and inadequate feeding remains one of the important causes of neonatal hypoglycemia. The mechanism by which these risk factors predispose a neonate for hypoglycemia may consist of decreased glycogen storage, increased utilization of glucose, decreased glycogenolysis or a combination of these mechanisms depending upon the etiology of neonatal hypoglycemia.^[2]

The neonates with hypoglycemia may commonly present with symptom signs and symptoms such as refusal to feed, lethargy, cyanosis, hypothermia, irregular respiration and apnea. Many neonates present with seizures. One of the important aspects of neonatal hypoglycemia is that in many instances of documented neonatal hypoglycemia the neonates remained completely asymptomatic. It is because of this reason that a high level of suspicion is needed to diagnose and treat cases of neonatal hypoglycemia. It is particularly important in neonates born to mothers with risk factors such as gestational diabetes mellitus and preterm neonates in whom there is

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increased risk of neonatal hypoglycemia. Neonatal hypoglycemia is fraught with the danger of catastrophic consequences in later life such as seizure disorder, delayed developmental milestones and mental retardation.^[3]

Once suspected the diagnosis can be confirmed by estimation of plasma glucose level and a value less than 47 mg/dL is usually taken as diagnostic of neonatal hypoglycemia. More advanced tests such as insulin levels (to rule out hyperinsulinemia as cause of neonatal hypoglycemia), urine ketones (for inborn error of metabolism) and imaging studies (for diagnosis is islet cell adenoma) are not usually done and are reserved for selected cases. Once the diagnosis is confirmed then the management is usually straight forward and consist of primary aim of correcting hypoglycemia and for this purpose continuous glucose infusion is started and the goal of management of hypoglycemia is to maintain blood glucose level of at least 45 mg/dl. In addition to maintenance of blood glucose level additional measures such as correction of acidosis, treatment of sepsis and management of shock must appropriately be done. Use of steroids and glucagon is usually reserved for cases with resistant hypoglycemia.^[4]

We conducted this prospective study to examine the risk factors predisposing neonates for incidence of hypoglycemia and clinical features of neonates with hypoglycemia.

MATERIALS AND METHODS

This was a prospective observational study conducted in the department of pediatrics of a tertiary care pediatric center situated in an urban area. 60 Neonates admitted in neonatal intensive care unit and found to have symptomatic hypoglycemia at the time of admission or during NICU stay were included in this study on the basis of a predefined inclusion and exclusion criteria. The diagnosis of neonatal hypoglycemia was made on the basis of blood glucose levels of less than 45 mg/dl. A detailed antenatal, natal and post-natal history was taken. Particular emphasis was given to the history of refusal to feed, lethargy and history of abnormal movements. Birth weight and gestational age at birth was also noted down. APGAR scores at birth in available in medical records were also noted to rule out possibility of birth asphyxia. Presence of risk factors such as maternal gestational diabetes, Pregnancy induced hypertension and intrauterine growth restriction were looked into and noted down. A complete blood count, micro ESR and CRP were done in all the cases. A detailed clinical examination was done. General examination followed by systemic examination was noted in a proforma. Rectal temperature was taken in all neonates. Symptomatic hypoglycemia was treated by initial bolus of 2 ml/kg of 10% dextrose followed by glucose infusion at a rate of 6 mg/kg/min. The rate

of infusion was increased on the basis of blood glucose levels in subsequent tests. SPSS 21.0 software was used for statistical purposes.

Inclusion Criteria:

1. Neonates who had symptomatic hypoglycemia at the time of admission or during NICU stay.
2. Documented Blood Glucose level less than 45 mg/dl.
3. Informed written consent was given by Parents or caretakers.

Exclusion criteria:

1. Parents or caregivers refused consent.
2. Serious comorbid conditions such as congenital heart diseases etc.

RESULTS

A total of 60 neonates were included in this study on the basis of a predefined inclusion and exclusion criteria. Out of these 60 neonates there were 35 males and 25 females with a M:F ratio of 1:0.71.

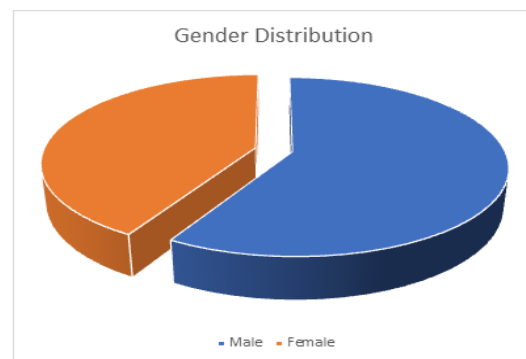


Figure 1: Gender Distribution of Neonates with Hypoglycemia.

The analysis of birth weight of the neonates showed that out of 60 cases majority of the cases were having low birth weight (37/60). Normal birth weight (<2.5 kg) was seen in 12 (20%) patients whereas very low birth weight (<1.5 kg) and extremely low birth weight were seen in 7 (11.67%) and 2 (3.33%) patients respectively. Macrosomia (>4kg) was seen in 2 (3.33%) cases.

Table 1: Birth weight of the studied cases

Birth Weight	No Of cases	Percentage
Extremely Low Birth Weight (< 1 kg)	2	3.33%
Very Low Birth Weight (< 1.5 kg)	7	11.67%
Low Birth Weight (< 2.5 kg)	37	61.67%
Normal Birth Weight (> 2.5 kg)	12	20 %
Macrosomia (> 4 kg)	2	3.33%
Total	60	100%

The neonates were divided into preterm, term and post term neonates on the basis of gestational age at

the time of delivery. 38 (63.33%) neonates were full term neonates (> 37 weeks) where was preterm (< 37 weeks) were 20 (33.33%). Post maturity (>42 weeks) was seen in 2 cases (3.33%).

Table 2: Gestational age of the studied cases.

Gestational age	No Of cases	Percentage
Preterm (< 37 weeks)	38	63.33%
Term (>37 weeks)	20	33.33%
Post Term (42 weeks and above)	2	3.33%
Total	60	100%

The analysis of maternal risk factors for the incidence of neonatal hypoglycemia showed that out of 60 neonates 22 (36.67%) neonates had some or the other maternal risk factors predisposing them for hypoglycemia. In 11 (18.33%) cases gestational diabetes was seen in mother whereas pre-eclampsia or eclampsia and Premature rupture of membranes were seen in 6 (10%) and 5 (10%) cases respectively.

Table 3: Maternal Risk Factors for neonatal hypoglycemia.

Maternal Risk Factors	No Of cases	Percentage
Gestational Diabetes	11	18.33 %
Pre-Eclampsia/Eclampsia	6	10.00 %
Premature rupture of membranes	5	8.33 %
Total	22	36.67 %

The analysis of neonatal risk factors showed that out of 60 studied cases neonatal risk factors were seen in 35 (58.33%) neonates. The most common neonatal risk factor was found to be birth asphyxia (26.67%) followed by septicemia (13.33%), hyperbilirubinemia (8.33%), meconium aspiration syndrome (5%) and polycythemia (5%).

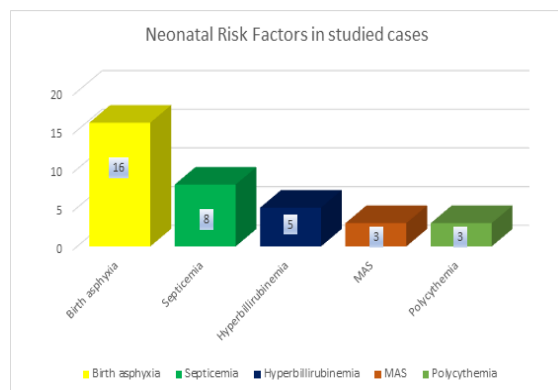


Figure 2: Neonatal Risk Factors for Neonatal Hypoglycemia.

The analysis of clinical features or presenting complaints showed that the most common presenting complaint was found to be refusal to feed which was seen in all the cases (100%). The other common presenting complaints were found to be lethargy (88.33%), abnormal movements/seizures (65%), respiratory distress (40%) and jaundice (8.33%).

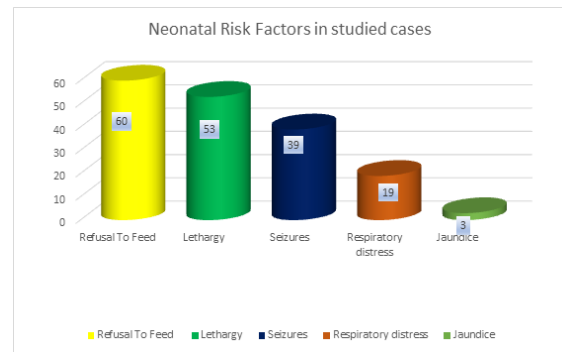


Figure 3: Presenting Complaints in neonates with Hypoglycemia.

DISCUSSION

In this study of 60 cases of neonatal hypoglycemia there were 35 males and 25 females with a M:F ratio of 1:0.71. This male preponderance was also reported by many authors. Rafiq A et al conducted a study to evaluate various maternal and fetal risk factors for neonatal hypoglycemia and its clinical presentation.^[5] The study found that Spectrum of clinical presentation included temperature instability 39%, jitteriness 34%, lethargy in 32%, cyanosis 12%, tachypnea 8%, apnea 6% and seizures 9%. Maternal risk factors for neonatal hypoglycemia noticed were maternal diabetic mellitus in, eclampsia, use of drugs like beta blockers, oral hypoglycemic agents, valproate, by mother and family history of metabolic disorder. Neonatal risk factors were hypothermia, endocrine disorder, inborn errors of metabolism, inadequate feeding 32%, low birth weight, small for gestational age, respiratory distress 31% and sepsis. Males were more commonly found to be affected as compared to female children. Similar male preponderance was also reported by the authors such as Saini A et al and Jonas D et al.^[6,7]

In our study majority of the cases with neonatal hypoglycemia were having low birth weight (<2.5 kg). Low birth weight seen in small for gestational age as well as preterm neonates is one of the important risk factors for development of hypoglycemia. Kumar TJ et al conducted an observational study of neonates with risk factors for hypoglycemia.^[8] The authors found that Out of 1883 Babies born with risk factors, 627 Babies developed at least one episode of hypoglycemia. Of these, 576 (30.3%) were asymptomatic hypoglycemia and 51 (3.0%) symptomatic hypoglycemia. Hypoglycemia was seen in 42% of small for gestational age, 33% of IDM, 19% of preterm and 10% of LGA babies. About 51% of newborns developed hypoglycemia at 2 hours of life and about 31% of newborns at 6 hours of life. No hypoglycemic episodes were noted after 24 hours of life. Similar findings were reported by the authors such as Phillips KG et al and Sharma A et al.^[9,10]

IN our study 22 (36.67%) neonates had some or the other maternal risk factors predisposing them for hypoglycemia. In 11 (18.33%) cases gestational diabetes was seen in mother whereas pre-eclampsia or eclampsia and Premature rupture of membranes were seen in 6 (10%) and 5 (10%) cases respectively. Bromiker R et al found that gestational age, maternal diabetes, low birth weight (<2500 g), and twin delivery were associated with early neonatal hypoglycaemia.^[11] Cornblath M reported that toxemia of pregnancy was one of the important risk factors for neonatal hypoglycaemia.^[12]

The study of neonatal risk factors for hypoglycemia showed that the most common neonatal risk factor was found to be birth asphyxia (26.67%) followed by septicemia (13.33%), hyperbilirubinemia (8.33%), meconium aspiration syndrome (5%) and polycythemia (5%). Stommaroska O et al conducted the study of 84 neonates with documented hypoglycaemia.^[13] The authors found that found that low birth weight was an important risk factor for incidence of hypoglycemia. Additionally, the authors found that hypoxic-ischemic encephalopathy (HIE) was found in 3 children (3.57%), infections in 22 (26.18%), respiratory distress syndrome (RDS) in 9 patients (10.62%), intracranial hemorrhage in 2 patients (2.38%). Similar findings were reported by the authors such as Schaefer-Graf UM et al,^[14] and Harris DL et al^[15]

CONCLUSION

Neonatal Hypoglycemia is one of the important causes of neonatal morbidity and mortality. Since in many cases the neonates with hypoglycemia present with subtle clinical findings it is important to keep a high index of suspicion particularly in neonates having risk factors for hypoglycemia.

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