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ORIGINAL RESEARCH ARTICLE

Clinical Profile and Risk Factors of Neonatal Hypoglycemia in Tertiary Care Teaching Hospital

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ABSTRACT

Introduction: Hypoglycemia is a frequent metabolic problem in the nursery and neonatal intensive care unit.[1] The majority of incidents of neonatal hypoglycemia are transient and represent typical glucose metabolism. Also, hypoglycemia signs may match those of various newborn illnesses. The aim of the study was to evaluate the clinical profile and risk factors of neonatal hypoglycemia in neonatal admitted to a tertiary care teaching hospital.

Materials and Methods: It was a prospective hospital-based study conducted in the Pediatric unit of Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, which is a tertiary care teaching hospital of the Rohilkhand region. All neonates were admitted to the Pediatric Department and bedside glucose levels <40 mg/dl were included. Initial blood glucose levels were checked by glucometer in *all* neonates within 2 hours of admission and once daily thereafter. Repeat testing was done whenever it was clinically indicated (lethargy, refusal to feed or new onset seizures) and in neonates with documented hypoglycemia at 2nd, 6th, 12th, 24th, 48th and 72nd hours of initial episode and management.

Results: The development of hypoglycemia was seen in babies born to mothers who had diabetes mellitus or gestational diabetes at a rate of 42.27%, eclampsia at a rate of 10.31%, and mode of delivery at a rate of 21.65% in the category of maternal risk factors. The prevalence of SGA (49.48%) was the factor that was related with hypoglycemia the most frequently. Lethargy (49.49%), jitteriness (47.42%), and seizures (42.27%) were the most prevalent manifestations found in infants who had the clinical presentation of hypoglycemia. Cyanosis was not observed in any neonate with hypoglycemia.

Conclusion: Hypoglycemia is the most preventable metabolic condition in neonates. The result showed that LBW, SGA, LGA, IDM/IGDM, newborns with respiratory distress, sepsis, hypothermia, and neonates with delayed and infrequent feeding had an increased risk of hypoglycemia. The most common presentation was lethargy, jitteriness and seizures among these neonates.

Keywords: Hypoglycemia, Neonatal, Glucose.

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INTRODUCTION

Hypoglycemia is a common metabolic issue in the neonatal critical care unit and nursery.[1] Hypoglycemia is defined as blood glucose levels <40 mg/dl. Excessive glucose use by the tissues or decreased generation causes it. Underdeveloped counter-regulatory systems cause neonatal hypoglycemia. Most occurrences are transitory and reflect normal glucose metabolism. Symptoms of hypoglycemia might resemble several other neonatal illnesses. Brain metabolism requires euglycemia. Symptoms of neonatal hypoglycemia may develop late; therefore, the absence of symptoms does not mean glucose concentration is adequate and brain metabolism is excellent. Hypoglycemia can be a result of metabolic or endocrine problems requiring treatment. Delayed identification and treatment of hypoglycemia causes neurological impairments, seizures, and mental retardation. Blood glucose levels change markedly within the first hour of life, making it important to know the exact age to diagnose hypoglycemia. The severing of the umbilical cord at birth interrupts the source of glucose. It's a failure to adapt to the extrauterine pattern of intermittent nutrient supply from the fetal state of continuous transplacental glucose consumption, leading to these changes. Maintenance of the normal blood glucose level in newborns depends on adequate glycogen stores, gluconeogenesis and maturation of pathways of glycogenolysis.

The operational threshold for hypoglycemia is a blood glucose value of <40 mg/dl or plasma glucose <45 mg/dl[2]. Plasma glucose <45 mg/dl in symptomatic newborn needs clinical interventions for increasing blood glucose levels and plasma glucose levels <36 mg/dl in asymptomatic requires intervention if symptoms appear or level do not increase even after feeding.[3]

Hypoglycemia can be symptomatic or asymptomatic, indicating the need for detailed history and examination.

Most findings are non-specific, which include abnormal respiratory patterns like apnea, tachypnea or respiratory distress. Cardiovascular signs like tachycardia or bradycardia, cyanotic episodes and neurologic features such as lethargy, jitteriness, weak suck, seizures, staring spells, somnolence and temperature instability.

Many risk factors for neonatal hypoglycemia have been identified which include prematurity, small for gestational age (SGA), low birth weight (LBW), macrosomia, perinatal stress (respiratory distress, sepsis, hypothermia, birth asphyxia), infant of a diabetic mother, inborn errors of metabolism, inadequate feeding or positive family history and maternal risk factors for neonatal hypoglycemia which are like eclampsia, maternal diabetes mellitus, intrapartum administration of glucose and uses of drugs like oral hypoglycemic agents, beta blockers and valproate, antenatal corticosteroids.

The study aims to know the clinical features and risk factors of neonatal hypoglycemia as there is a paucity of data from western Uttar Pradesh.

MATERIALS AND METHODS

It was a prospective hospital-based study, conducted in the Pediatric unit of Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, which is a tertiary care teaching hospital of the Rohilkhand region. All neonates admitted to the Pediatric Department and in whom bedside blood glucose (by glucometer) values <40 mg/dl, were included in the study as per the inclusion criteria. Initial blood glucose levels were checked by glucometer in *all* neonates within 2 hours of admission and once daily thereafter and repeat testing was done, when clinically indicated (lethargy, refusal to feed or new onset seizures) and in neonates with documented hypoglycemia at 2^{nd}, 6^{th}, 12^{th}, 24^{th}, 48^{th} and 72^{nd} hours of initial episode and management.

The study was done after ethical clearance from the Institutional Ethical Committee (IEC). A written informed consent was taken from the parents. A detailed clinical history, including demographic data like sex, date of admission, day of life, weight, and gestational age was taken. The clinical examination of all newborns diagnosed with neonatal hypoglycemia was done and details were noted in the proforma.

Statistical Analysis

The sample size was decided on the basis of the formula (Z1-α/2)2pq/e2, where p is the prevalence, q=1-p and e is the working error. A working error of 10% has been assumed. The total neonates taken into the study were 97 taking prevalence as 42% over a period of 1.5 years in the Inpatient, Department of Pediatrics of SRMS IMS. The data were recorded, compiled using Microsoft® Excel worksheet (version 2019) and subjected to statistical analysis using SPSS (SPSS 21.0, IBM, Armonk, NY, United States of America). Data were expressed as frequency, percentages, and mean.

Table 1: Baseline characteristics

Baseline characteristics	*Frequency (N = 97)*	*Percentage*
Number of episode		
Single hypoglycemic episodes	62	63.92
Multiple hypoglycemic episodes	35	36.08
Gender		
Male	56	57.73
Female	41	42.26

RESULTS

Out of total 97 neonates enrolled in this sudy, 63.92% had a single episode of hypoglycemia, while 36.08% had multiple episodes of hypoglycemia. 57.73% were males and 42.26% were females and M: F ratio was 1.3:1.

Maternal Risk Factors

Maternal risk factors were evaluated in the hypoglycemic babies. It was observed that babies born to mothers with gestational diabetes and diabetes mellitus (42.27%) had the maximum frequency of hypoglycemia, which was followed by mode of delivery (21.65%).

Other Neonatal Risk Factors

SGA (49.48%) was the most common risk factor associated with hypoglycemia, whereas shock (1.03%) was the least responsible factor.

Hypoglycemia in Relation to Clinical Features

Among clinical manifestations of hypoglycemia, lethargy (49.49%) was observed in maximum neonates, apnea was the minimum observed symptom (2.06%) in neonatal hypoglycemia, whereas cyanosis was not seen in any neonate with hypoglycemia.

DISCUSSION

Hypoglycemia is the most common metabolic problem seen in neonates. It merely reflects a normal adaptation process to extrauterine life in most cases. It has been almost a century since hypoglycemia was first described

Table 2: Maternal risk factor

Maternal risk factor	*Frequency (N = 97)*	*Percentage*
Eclampsia	10	10.31
Diabetes mellitus	41	42.27
Drug Uses	0	-
Maternal tocolytic therapy	0	-
Mode of delivery	21	21.65

Table 3: Other neonatal risk factor

Other neonatal risk factors	*Frequency (N = 97)*	*Percentage*
Perinatal asphyxia	5	5.15
Syndromic child	0	-
Prematurity	37	38.14
IEM	5	5.15
Exchange transfusion	2	2.06
SGA	48	49.48
Sepsis	17	17.53
Shock	1	1.03
Respiratory distress	40	41.24
Polycythemia	2	2.06

Table 4: Hypoglycemia in relation to clinical features

	Frequency (N = 97)	*Percentage*
Jitteriness	46	47.42
Lethargy	48	49.48
Tachypnea	40	41.24
Apnea	2	2.06
Seizures	41	42.27
Refusal to feed	4	4.12
Abnormal cry	5	5.15
Altered sensorium	0	-
Limpness	13	13.40
LBW	46	47.42
Sepsis	17	17.53
Hypothermia	18	18.56
Irritability	13	13.40
Cyanosis	0	-
Exaggerated moro's reflex	6	6.19

in children and approximately more than 50 years since it was first described in newborns. Glucose is the major source of energy to the body and a major source of energy to the brain. As the placenta is the major source of glucose to the neonate in utero, after birth and cutting of the umbilical cord, the baby has to convert to other ways of replenishing its glucose stores.

Out of a total 97 neonates, 63.92% had a single episode of hypoglycemia, while 36.08% had multiple episodes of hypoglycemia (Table 1). 57.73% were males and 42.26% were females and M: F ratio was 1.3:1. In a study by Somanathan *et al.*,[4] among the 220 neonates with hypoglycemia, 137 (62.3%) were males and 83 (37.7%) were females. In a study by Yunarto *et al.*,[5] 52% of hypoglycemic neonates were males and 48% hypoglycemic neonates were females.

Maternal risk factors were evaluated in the hypoglycemic babies (Table 2). It was observed that babies born to mother with gestational diabetes and diabetes mellitus (42.27%) had the maximum frequency of hypoglycemia which was followed by mode of delivery (21.65%).GDM was also a common maternal risk factor in studies done by Manjunatha BR *et al.*[6], Bhand SA *et al.*[7], Singh K *et al.*[3] and Singh YP *et al.*[8] Pre-eclampsia was also present in Amarendra M[9], Singh YP *et al.*, Manjunatha BR *et al.*[6], Singh K *et al*[3] and Bhand SA *et al.*[7] but it was not so in our study, may be due to a smaller number of mothers with pre-eclampsia in our study. According to Cornblath M *et al.*[10], maternal risk factor for neonatal hypoglycemia is arterial hypertension. While in the study done by Burdan DR *et al.*[11], showed urinary tract infections and rupture of membrane as maternal risk factors for neonatal hypoglycemia. PROM as a maternal risk factor was present in the study done by Singh K *et al.* and Amarendra M *et al.*[9], but we did not consider it in our study. Stage 2 prolonged labor can also produce hypoglycemia over two-thirds of neonates with hypoglycemia and one or more newborn risk factors documented by P. K. Singhal *et al.* study.[12]

SGA (49.48%) was the most common risk factor associated with hypoglycemia (Table 3). In a study by Somanathan *et al.*,[4] the neonatal risk factors associated with hypoglycemia were prematurity 28.2%), SGA (29.5%), LGA (5.9%), IDM (20.4%) and comorbidities (sepsis, birth asphyxia, polycythemia and shock) were present in 16.3% of the hypoglycemic neonates. Among the comorbid condition birth asphyxia was present in 12 (5.4%), sepsis in 19 (8.6%), polycythemia in 4 (1.8%) and shock in1 (0.45%). 84% of the hypoglycemic neonates had at least one risk factor.

Lethargy (49.49%) was observed in maximum number of hypoglycemic neonates whereas apnea was the minimum observed symptom (2.06%)(Table 4). In a study by Somanathan *et al.*,[4] out of 220 children with hypoglycemia 136 (61.8%) were asymptomatic and 84 (38.2%) presented with symptoms. The common symptoms were poor feeding (69%), lethargy (17.8%), jitteriness (11.9%), convulsions (9.5%), irritability (4.7%), hypotonia (2.3%) and cyanosis (1.2%). 29% of neonates presented with hypoglycemia on day 1 of life, 26.8% of neonates on day 2, 21.4% on day 3 and 22.7% beyond 72 hours of life.

CONCLUSION

Hypoglycemia is the most common preventable metabolic abnormality seen in neonates in developing countries. It was observed that LBW, especially small for dates, LGA, IDM/IGDM, neonates with respiratory distress, sepsis, hypothermia, and neonates with delayed and infrequent feeds are at increased risk of hypoglycemia. The most common presentation was lethargy, jitteriness and seizures among these neonates. Sometimes it also presents with no symptoms. So, there is need for

aggressive blood glucose monitoring and management to reduce early infant mortality and neurodevelopmental sequelae.

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