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Original Article

Risk factors of neonatal hypoglycemia

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Abstract

Background Hypoglycemia is the most common metabolic issue in newborns and should be treated as soon as possible to prevent complications of neurologic impairment, mental retardation, developmental delay, and cardiovascular disorders.

Objective To assess maternal, fetal, and neonatal factors for identifying infants at risk of developing neonatal hypoglycemia.

Methods This case-control study was conducted in the Perinatal Unit of Dr. Kariadi Hospital, Semarang, Central Java. A total of 123 newborns with blood glucose <47 mg/dL comprised the case group and 123 newborns without hypoglycemia comprised the control group. Characteristics of infants, maternal age, maternal pregnancy-related conditions, as well as fetal and neonatal factors were recorded and analyzed for possible relationships with hypoglycemia.

Results Out of 677 newborns, hypoglycemia was found in 123 (18.2%) infants (59 male, 64 female). In hypoglycemic group, 47.1% were preterm, 30.9% very preterm, and 6.5% extremely preterm infants. Factors associated with neonatal hypoglycemia were prematurity (OR 6.537; 95%CI 3.543 to 12.063; P <0.001), low birth weight (OR 2.979; 95% CI 1.532 to 5.795; P<0.001), small for gestational age (OR 1.805; 95% CI 1.054 to 3.095; P=0.031), and birth asphyxia (OR 3.386; 95% CI 1.945 to 5.895; P<0.001). In multivariate regression analysis, prematurity and low birth weight remained the significant factors associated with neonatal hypoglycemia.

Conclusion Prematurity and, low birth weight are significant risk factors associated with neonatal hypoglycemia. Routine screening and monitoring of blood glucose is recommended for preterm newborns and infants with low birth weight. [**Paediatr Indones. 2019;59:252-6; doi: http://dx.doi.org/10.14238/pi59.5.2019.252-6**].

Keywords: *neonatal hypoglicemia; birth asphyxia; low birth weight; small for gestational age; prematurity*

Hypoglycemia is the most common metabolic issue in newborns and should be treated as soon as possible to prevent complications of neurological impairment, mental retardation, developmental delay, and debilitating cardiovascular function.[1] It is important to recognize hypoglycemia in order to initiate prompt treatment and prevent long-term neurologic damage. Hypoglycemia is mostly asymptomatic, but timely and accurate recognition is important to achieve optimal neonatal outcomes.[2] We aimed to assess maternal, fetal, and neonatal factors for identifying infants at risk of developing neonatal hypoglycemia.

Methods

This case-control study was conducted in the Perinatal Unit of Dr. Kariadi Hospital, Semarang, Central Java, Indonesia. Data were obtained from medical records of infants born in 2017. Fullterm was defined as baby born after 37 weeks of pregnancy; meanwhile, preterm was defined as baby born before 37 weeks of pregnancy and divided into very preterm (28-32 weeks) and extremely preterm (less than 28

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weeks). Babies born with birthweight between 2500 - 3999 g were considered as normal birthweight; low birth weight (LBW) was defined as a birth weight of less than 2500 g which further categorized into very low birth weight (<1500 g) and extremely low birth weight (<1000 g). Birth asphyxia was defined as the failure to establish breathing at birth defined based on the 5th min Apgar score of <7. Blood glucose levels documented in medical records were measured from a heel puncture blood sample.

Patients born to diabetic mothers or with multiple congenital anomalies were excluded. A total of 123 newborns with blood glucose <47 mg/dL comprised the case group. The control group was comprised of 123 newborns without hypoglycemia, included by simple randomization sampling. Characteristics of infants, maternal age, maternal pregnancy-related conditions, as well as fetal and neonatal factors were recorded. Data were analyzed using *SPSS 20* for Windows software. Means and proportions of blood glucose levels and basic socio-demographic data, as well as clinical data, were analyzed by Student's T-test and Chi-square test, respectively. Multivariate analysis was performed to identify significant risk factors related to the occurrence of hypoglycemia. Results with P values < 0.05 were considered to be statistically significant.

The Medical and Health Research Ethics Committee of Dr. Kariadi Hospital approved this study.

Results

Characteristics of subjects are shown in **Table 1**. Of 677 newborns hospitalized in year 2017, hypoglycemia was found in 123 (18.2%) infants (59 male, 64 female). Of the case group, a total of 65 (52.8%) were born via caesarean delivery, maternal age were mostly <35 years (79.7%), and multiparous (65%).

Table 2 shows that in the case group, hypoglycemia was found mostly in infants born less than 37 weeks consisted of 58 (47.1%) preterm, 38 (30.9%) very preterm, and 8 (6.5%) extremely preterm infants. A total of 89 (72.3%) were born with low birth weight, 25 (20.3%) were born very low birth weight, and 5 (4%) infants were born with extremely low birth weight. In addition, 49 (39.9%) infants were born small for gestational age (SGA). Factors associated with neonatal hypoglycemia were prematurity (OR 6.537; 95% CI 3.543 to 12.063; P<0.001), birth weight less than 2,500 g (OR 2.979; 95%CI 1.532 to 5.795; P<0.001), SGA (OR 1.805; 95%CI 1.054 to 3.095; P=0.031), and birth asphyxia (OR 3.386; 95%CI 1.945 to 5.895; P<0.001).

Multivariate regression analysis as shown in **Table 3** revealed that prematurity and low birth weight were the significant factors associated with neonatal hypoglycemia. None of the other maternal or fetal conditions were associated with the occurrence of neonatal hypoglycemia in our study.

Table 1. Characteristics of subjects

Characteristics	Hypoglycemic (n = 123)	Normoglycemic (n = 123)	P value
Gender, n (%)			
Male	59 (48)	48 (39)	0.158
Female	64 (52)	75 (61)	
Mode of delivery, n (%)			
Caesarean	65 (52.8)	76 (61.8)	0.157
Vaginal	58 (47.2)	47 (38.2)	
Maternal age, n (%)			
≥35 years	25 (20.3)	26 (21.2)	0.875
<35 years	98 (79.7)	97 (78.8)	
Maternal parity, n (%)			
Primiparous	43 (35)	42 (34.1)	0.89
Multiparous	80 (65)	81 (65.8)	

Table 2. Risk factors for neonatal hypoglycemia

Variables	Hypoglycemic (n = 123)	Normoglycemic (n = 123)	Odds ratio (95% CI)	P value
Birth weight to gestational age, n (%)				
SGA	49 (39.9)	33 (26.8)	1.805 (1.054 to 3.095)	0.031*
AGA	74 (60.1)	90 (73.2)		
Gestational age, n (%)				
Full term	19 (15.4)	64 (52)	6.537 (3.543 to 12.063)	<0.001*
Preterm	58 (47.1)	42 (34.1)		
Very preterm	38 (30.9)	13 (10.6)		
Extremely preterm	8 (6.5)	4 (3.2)		
Birth weight, n (%)				
NBW	4 (3.2)	37 (30.1)	2.979 (1.532 to 5.795)	0.001*
LBW	89 (72.3)	79 (64.2)		
VLBW	25 (20.3)	4 (3.2)		
ELBW	5 (4)	3 (2.4)		
Maternal risk factors, n (%)				
PROM	14 (11.4)	14 (11.4)	1.000 (0.455 to 2.197)	1.000
Preeclampsia/ eclampsia	35 (26)	40 (32.5)	0.825 (0.479 to 1.422)	0.489
Placental abnormality	9 (7.3)	5 (4)	1.863 (0.606 to 5.728)	0.278
Maternal infection	5 (4)	10 (8.1)	0.479 (0.159 to 1.444)	0.191
Fetal risk factors, n (%)				
Fetal distress	8 (6.5)	5 (4)	1.642 (0.522 to 5.167)	0.397
IUGR	31 (25.2)	52 (42.3)	1.637 (0.879 to 3.047)	0.120
Gemelli	13 (10.6)	8 (6.5)	1.699 (0.678 to 4.257)	0.258
Neonatal risk factors, n (%)				
Birth asphyxia	60 (48.8)	27 (22)	3.386 (1.945 to 5.895)	<0.001*
Neonatal jaundice	8 (6.5)	24 (19.5)	0.287 (0.123 to 0.667)	0.004
Infection	12 (9.8)	6 (4.8)	2.108 (0.765 to 5.810)	0.149
RDS	4 (3.2)	2 (1.6)	2.034 (0.366 to 11.313)	0.418

NBW=normal birth weight; LBW=low birth weight; VLBW=very low birth weight; ELBW=extremely low birth weight; PROM=premature rupture of the membrane; HELLP=hemolysis, elevated liver enzyme levels, and low platelet levels; IUGR=intrauterine growth restriction; RDS=respiratory distress syndrome

Table 3. Multivariate logistic regression of risk factors for neonatal hypoglycemia

Variables	Odds ratio (95% CI)	P value
Gestational age	7.943 (3.911 to 16.130)	<0.001*
Birth weight	3.833 (1.690 to 8.692)	0.001*
Mode of delivery	0.752 (0.406 to 1.393)	0.365
Birth weight to gestational age	0.905 (0.357 to 2.294)	0.833
Maternal heart disease	0.545 (0.123 to 2.417)	0.424
Maternal infection	0.685 (0.180 to 2.604)	0.578
IUGR	1.630 (0.554 to 4.792)	0.374
Birth asphyxia	1.828 (0.898 to 3.724)	0.096
Neonatal jaundice	0.618 (0.228 to 1.675)	0.345
Neonatal infection	1.576 (0.482 to 5.157)	0.452

Discussion

Among infants born at <37 weeks, we observed an increased risk of neonatal hypoglycemia. The incidences of hypoglycemia among preterm, very preterm, and extremely preterm newborns in our study were 47.1%, 30.9%, and 6.5%, respectively. The prevalence of hypoglycemia in our study was higher than that of Bromiker *et al.*,[2] however, they found that prematurity as the strongest risk factor for neonatal hypoglycemia. Preterm neonates are at risk of developing hypoglycemia and its associated complications due to their low reserve of glycogen and fat stores, inefficient production of glucose using gluconeogenesis pathways, higher metabolic requirement due to a relatively larger brain size, and inadequate ability to escalate a counter-regulatory response to hypoglycemia.[3]

Birth weight was found to be one of the significant risk factors associated with hypoglycemia in our study. In hypoglycemic infants, 72.3%, 20.3%, and 4% were LBW, VLBW, and ELBW infants, respectively. Similarly, Kumar *et al.*[4] reported a higher percentage LBW babies in their hypoglycemic group (64% LBW *vs.* 14% NBW). They found that LBW infants were susceptible to developing hypoglycemia mainly in first 24 hours of life, with late introduction of breastfeeding being an additional risk. Low birth weight neonates are born with low stores of glycogen and adipose tissues as well as inadequate capacity to produce glucose through the gluconeogenesis pathway or disproportionate peripheral tissue utilization of glucose. Hence, such infants are prone to hypoglycemia.[3]

Hypoglycemia was present in 59.8% of the SGA infants. These findings were consistent with those of Ho *et al.*[5] who reported an incidence of 34.2% in SGA infants. The neonatal brain and vital organs need a steady supply of glucose to meet nutritional demands. In full term and healthy neonates, this is accomplished by hormonal and metabolic adaptive changes. Preterm and SGA neonates are prone to hypoglycemia due to their limited glucose storage, insufficient adaptive changes, and underdeveloped metabolic pathways.[6]

A previous study reported lower cord blood glucose levels in Caesarean-delivered newborns.[7] However, we found no significant difference in Caesarean-delivered vs. vaginally-delivered newborns for the two groups. This finding might have been due to the limited sample size of our study and the different method of measuring the blood glucose level as we took the samples from peripheral blood specimen.

Of hypoglycemic infants, 48.8% had birth asphyxia. The risk of developing hypoglycemia increased three-fold compared to vigorous-born infants. A previous study reported an incidence of 26.86% hypoglycemia among infants born with birth asphyxia.[8] During asphyxia, an increased anaerobic glycolysis rate along with glycogenolysis predisposes neonates to hypoglycemia.[9]

The main limitation of this study was its susceptibility to information bias, as data collected reflected what was recorded in the medical charts. Many factors may affect the prevalence of neonatal hypoglycemia in different medical centers. Thus, performing a hospital-based study in this regard is important to establish comprehensive neonatal care guidelines to reduce neonatal mortality and morbidity caused by hypoglycemia among newborns at risk.

In conclusion, prematurity and low birth weight are significant risk factors associated with neonatal hypoglycemia. Routine screening and monitoring of blood glucose is recommended for preterm newborns and infants with low birth weight.

Conflict of Interest

None declared.

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