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Risk factors of neonatal hypoglycemia in Banda Aceh: A Retrospective Cross-Sectional Study

Faktor risiko hipoglikemia neonatal di Banda Aceh: Studi potong lintang retrospektif

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Abstract

Hypoglycemia is the most common metabolic disorder in newborns during the first two days of life, with a global prevalence of 5-15% in at-risk populations. This condition can cause permanent neurological damage and intellectual disabilities. Objective: To analyze the risk factors of neonatal hypoglycemia at Dr. Zainoel Abidin Hospital, Banda Aceh. Methods: This retrospective cross-sectional study used medical records from January to December 2024. The key predictors included gestational age, birth weight, maternal diabetes mellitus, eclampsia, and delivery mode. All eligible records (n=448) were included. Data were analyzed using SPSS version 29 with the chi-square test and multiple logistic regression. Hypoglycemia (blood glucose <45 mg/dL within 24 h of birth) was found in 67 (15.0%) infants. Multivariate analysis identified cesarean section as the strongest independent predictor (AOR=3.850; p<0.001), followed by birth weight <2500 g (AOR=6.345; p=0.004), and prematurity <37 weeks (AOR=3.383; p=0.001). In conclusion, cesarean delivery, prematurity, and low birth weight were independent risk factors for neonatal hypoglycemia after multivariate adjustment.

Keywords: Neonatal hypoglycemia, low birth weight, cesarean section, prematurity, risk factors, maternal diabetes

Abstrak

Gangguan metabolik tersering yang dialami neonatus dalam dua hari awal kehidupan adalah hipoglikemia, dengan prevalensi global berkisar 5-15% pada populasi berisiko. Kondisi ini berpotensi menimbulkan kerusakan neurologis permanen dan keterbatasan fungsi intelektual. Studi ini bertujuan untuk menganalisis berbagai faktor risiko hipoglikemia pada neonatus di RSUD Dr. Zainoel Abidin Banda Aceh. Metode, desain penelitian potong lintang retrospektif memanfaatkan data rekam medis selama periode Januari-Desember 2024. Prediktor utama meliputi usia gestasi, berat badan lahir, diabetes mellitus maternal, eklampsia, dan metode persalinan. Seluruh rekam medis yang memenuhi kriteria (n=448) diikutsertakan. Pengolahan data dilakukan melalui SPSS versi 29 menggunakan uji chi-square dan analisis regresi logistik berganda. Hasil, hipoglikemia (glukosa darah <45 mg/dL dalam 24 jam setelah lahir) didapatkan pada 67 (15,0%) subjek. Uji multivariat menunjukkan sectio caesar sebagai prediktor independen terkuat (AOR=3,850; p<0,001), kemudian berat badan lahir <2500 gram (AOR=6,345; p=0,004), dan prematuritas <37 minggu (AOR=3,383; p=0,001). Kesimpulan, sectio caesar, prematuritas, dan berat badan lahir rendah merupakan faktor risiko independen hipoglikemia neonatal setelah penyesuaian multivariat.

Kata Kunci: Hipoglikemia neonatal, berat badan lahir rendah, sectio caesar, faktor risiko, diabetes maternal, prematuritas

Introduction

The fetal and neonatal brains predominantly rely on glucose as their primary energy substrate. Hypoglycemia is a frequent metabolic maladaptation in newborns, typically manifesting within the initial days post-delivery as infants transition to extrauterine life, presenting with non-specific clinical features or remaining clinically silent, stemming from an imbalance between insufficient glucose supply due to reduced endogenous production or heightened consumption of glycemic reserves (Hubbard & Hay, 2021; Chen et al., 2022; Gu et al., 2019).

The precise threshold for defining neonatal hypoglycemia continues to be debated, with insufficient evidence-based consensus. Current American Academy of Pediatrics (AAP) recommendations establish diagnostic criteria for blood glucose concentrations below 40 mg/dL during the initial four hours post-birth or below 45 mg/dL between four and twenty-four hours of age. This study adopted the AAP cutoff of <45 mg/dL within 24 h of birth, given its wide acceptance and clinical applicability in settings without continuous glucose monitoring (Adamkin, 2017; Anderson et al., 2023).

The pathophysiological basis of neonatal hypoglycemia encompasses diminished hepatic glycogen reserves, insufficient muscular protein stores serving as amino acid substrates for gluconeogenesis, and inadequate adipose tissue providing fatty acid precursors. Despite frequently being clinically silent or presenting with non-distinctive manifestations, neonatal hypoglycemia can be anticipated by recognizing established risk determinants. The AAP characterizes vulnerable populations as including premature neonates, growth-restricted infants, and offspring of mothers with diabetes mellitus (Cumming et al., 2022; Hosagasi et al., 2018; Shah et al., 2019).

Bromiker et al. (2019) documented a hypoglycemia prevalence rate of 12.1% among newborns. Harris and collaborators (2020), utilizing AAP criteria, determined that one-quarter of all births carried hypoglycemia risk, with approximately half of these vulnerable infants experiencing at least one hypoglycemic episode. Investigation by Dr. Sikandar Ali Bhand and associates (2019) identified correlations between hypoglycemia and various neonatal determinants, including reduced birth weight, restricted intrauterine growth, excessive fetal size, pulmonary compromise, infectious processes, thermal instability, cardiac malformations, suboptimal nutrition, alongside maternal contributors such as hypertensive disorders, diabetic conditions, and pharmaceutical exposures.

Observations in 2017 at the Perinatal Unit of Dr. Kariadi Hospital, Semarang, Central Java, Indonesia, showed that hypoglycemia was most commonly observed in 123 (18,2%) infants, comprising 59 males and 64 females (Yunarto & Sarosa, 2019).

Furthermore, there is a lack of regional data from Aceh Province that could reflect the local demographic and clinical characteristics influencing neonatal hypoglycemia. To our knowledge, no previous study has systematically analyzed cesarean delivery as a risk factor for neonatal hypoglycemia in this region.

This study addresses these gaps by comprehensively analyzing both neonatal (gestational age, birth weight, APGAR score, and body temperature) and maternal factors (diabetes mellitus, eclampsia, obesity, and delivery method) simultaneously using multivariate analysis. The novelty of this research lies in its comprehensive approach to identifying the dominant risk factors specific to the population at Dr. Zainoel Abidin Hospital, Banda Aceh, which serves as a tertiary referral center for the Aceh province. Additionally, this study provides the first systematic analysis of cesarean delivery as a risk factor for neonatal hypoglycemia in this region. This area has received limited attention in previous studies in Indonesia.

The results of this study are expected to provide information on hypoglycemia in neonates at Dr. Zainoel Abidin Hospital, Banda Aceh, which will enable better prognostication based on risk factor analysis, diagnosis, and appropriate management of hypoglycemia. Furthermore, the findings will inform evidence-based screening protocols and preventive strategies tailored to the local population, ultimately improving neonatal outcomes and reducing morbidity associated with hypoglycemia in the future.

Methods

Study Design and Setting

This retrospective observational analytical study utilized a cross-sectional framework at Dr.

Zainoel Abidin Hospital Banda Aceh, accomplished through the compilation of neonatal patient information from Dr. Zainoel Abidin Hospital Banda Aceh, a tertiary referral center. Data extraction will occur between September and December 2024, covering records from January 1 to December 31, 2024.

Population and Sampling

The study population included all neonates born at the Dr. Zainoel Abidin Hospital during the study period. The inclusion criteria were neonates with complete medical records containing all the study variables. The exclusion criteria were incomplete data and diagnosed congenital metabolic disorders. The initial sample size calculation using the Lemeshow formula (95% CI, 18.2% proportion, 10% margin of error) yielded a minimum of 64 samples. As all 448 eligible records were accessible and met the criteria, the entire population was included in the analyses.

Data Collection Procedure

Data were collected from medical records by trained research assistants using a standardized data extraction form. The following variables were collected: (1) neonatal characteristics: sex, gestational age (weeks), birth weight (grams), APGAR score at 5 minutes, body temperature at admission, and blood glucose level within 24 hours of birth; (2) maternal characteristics: age (years), body weight status, history of diabetes mellitus, history of eclampsia, and delivery method. All data were verified by cross-checking with the nursing notes and laboratory records to ensure accuracy.

Outcome and Predictor Definitions

The primary outcome was neonatal hypoglycemia, defined as a blood glucose concentration of <45 mg/dL within 24 h of birth, measured via point-of-care glucometry following AAP criteria. The predictor variables were categorized as follows: gestational age (preterm: <37 weeks; term: 37-40 weeks; post-term: >40 weeks), birth weight (low birth weight: <2500 g; normal: 2500-4000 g; macrosomia: >4000 g), APGAR score (low: <7; normal: ≥7), and body temperature (hypothermia: <36.5°C; normothermia: ≥36.5°C).

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 29. Descriptive statistics are presented as frequencies and percentages for categorical variables. Bivariate analysis was performed using the chi-square test for variables with expected cell counts ≥5 and Fisher's exact test for variables with expected cell counts <5 (maternal diabetes mellitus and obesity). Variables with p-values ≤0.05 in the bivariate analysis were entered into the multivariate logistic regression analysis using the enter method. Collinearity among independent variables was assessed using the Variance Inflation Factor (VIF), with values <5 considered acceptable. The model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test. Results are presented as crude odds ratios (OR) and adjusted odds ratios (AOR) with 95% confidence intervals.

Ethical Considerations

Ethical clearance was obtained (271/ETIK-RSUDZA/2024). Patient data were anonymized with secure storage and restricted access.

Result and Discussion

Baseline Characteristics

This study was conducted by collecting data from the medical records of infants born at Dr. Zainoel Abidin Hospital Banda Aceh, both those treated in the NICU and Perinatology, during the specified research period with a total of 448 subjects.

Table 1. Baseline characteristics of study subjects

Characteristics	n	%
Gender		
Male	235	52.5
Female	213	47.5
Birth Weight		
< 2500 g	205	45.8
2500–4000 g	222	49.5
> 4000 g	21	4.7
Gestational Age		
< 37 weeks	153	34.2
37–40 weeks	282	62.9
> 40 weeks	13	2.9
APGAR Score		
< 7	218	48.7
≥ 7	230	51.3
Body Temperature		
Hypothermia	40	8.9
Normothermia	408	91.1
Delivery Method		

Cesarean section	288	64.3
Vaginal delivery	160	35.7
Blood Glucose Level		
Hypoglycemia	67	15.0
Normoglycemia	381	85.0

Based on Table 1, of the 448 study participants, the majority were male (52,5%) with a birth weight of 2500-4000 grams (49,6%), followed by low birth weight <2500 grams (45,8%) and birth weight >4000 grams (4,7%). In terms of gestational age, which was divided into three groups, term infants (37-40 weeks) were predominant (62,9%). Based on Apgar scores, the samples were evenly distributed with <7 (48,7%) and >7 (51,3%). The majority had a cesarean section (CS) delivery history (64,3%) and normothermic body temperature (91,1%). In terms of blood glucose levels, 85% of the subjects had normoglycemia and 15% had hypoglycemia.

Table 2. Maternal risk factors characteristics

Characteristics	n	%
Maternal Age		
< 35 years	335	74.8
≥ 35 years	113	25.2
Body Weight Status		
Normal	441	98.4
Obesity	7	1.6
Diabetes Mellitus		
Yes	9	2.0
No	439	98.0
Eclampsia		
Yes	22	4.9
No	426	95.1

In terms of maternal risk factors (Table 2), of the 448 subjects, maternal age <35 years was more predominant (74.8%) with normal body weight (98.4%). Of all the samples, only 2.0% had DM and 4.9% had eclampsia.

Association of Risk Factors with the Incidence of Neonatal Hypoglycemia

Table 3. Analysis of risk factors associated with neonatal hypoglycemia

Variables	Status		OR	95% CI	p-value
	Hypoglycemia n (%)	Normoglycemia n (%)			
Gestational Age					
< 37 weeks	29 (19,0)	124 (81,0)	-		0,048
37–40 weeks	34 (12,1)	248 (87,9)	1,706	0,99–2,93	0,053
> 40 weeks	4 (30,8)	9 (69,2)	0,526	0,15–1,83	0,312
Birth Weight					
< 2500 grams	23 (11,2)	182 (88,8)	4,870	1,82–12,99	0,002
2500-4000 grams	36 (16,2)	186 (83,8)	3,179	1,23–8,22	0,017
>4000 grams	8 (38,1)	13 (61,9)	-		0,006
Apgar Score					
< 7	33 (15,1)	185 (84,9)	1,042	0,61–1,72	0,999
≥ 7	34 (14,8)	196 (85,2)			
Body Temperature					
Hypothermia	9 (22,5)	31 (77,5)	1,583	0,79–3,87	0,242
Normothermia	58 (14,2)	350 (85,8)			
Mother's Age					
< 35 years	17 (14,2)	103 (85,8)	0,929	0,51–1,66	0,894
≥ 35 years	50 (15,2)	278 (84,8)			
Maternal Body Weight					
Obesity	2 (28,6)	5 (71,4)	1,938	0,44–12,18	0,628
Normal	65 (14,7)	376 (85,3)			
Diabetes Mellitus					
Yes	4 (44,4)	5 (55,6)	3,097	1,25–18,26	0,042
No	63 (14,4)	376 (85,6)			
Eclampsia					
Yes	9 (40,9)	13 (59,1)	3,005	1,79–10,78	0,001
No	58 (13,6)	368 (86,4)			

Birth History					
Cesarean Section	31 (10,7)	258 (89,3)	3,625	2,91–8,92	0,000
Vaginal Delivery	36 (22,6)	123 (77,4)			

Bivariate statistical examination revealed no meaningful correlation between Apgar score (p = 0.999), body temperature (p = 0.242), maternal age (p = 0.894), and maternal body weight (p = 0.628) and neonatal hypoglycemia. Fisher's exact test was applied for maternal DM and obesity because of expected cell counts <5. Among 9 examined variables, 5 variables demonstrated significant associations (p<0.05) with neonatal hypoglycemic occurrence: gestational age (p = 0.048; reference: 37-40 weeks) with age <37 weeks presenting elevated risk (OR=1.70; 95% CI: 0.99-2.93), birth weight >4000 grams presenting elevated risk (p = 0.006; OR=4.87; 95% CI: 1.82-13.0; reference: <2500 grams), mothers with diabetes mellitus (p = 0.042; OR=4.77; 95% CI: 1.25-18.3), mothers with eclampsia (p = 0.001; OR=4.39; 95% CI: 1.79-10.8), and cesarean delivery method (p<0.001; OR=2.42; 95% CI: 1.44-4.07). Notably, gestational age <37 weeks showed borderline significance, with a confidence interval of 1.

Determinants of Risk Factors for Neonatal Hypoglycemia

Multivariate analysis was performed on variables with p-values < 0.05 to assess the simultaneous effects of risk factors on the incidence of neonatal hypoglycemia. Five risk factors met the statistical requirements for multivariate analysis using multiple logistic regression analysis: gestational age, birth weight, mothers with DM, mothers with eclampsia, and history of cesarean section delivery.

Table 4. Determinants of risk factors for neonatal hypoglycemia

Independent Variables	Coefficient	OR	95% CI	p-value
Gestational Age				0.006
37-40 weeks	1.219	3.383	1.59–7.16	0.001
>40 weeks	0.914	2.648	0.55–12.65	0.222
Birth Weight				0.005
<2500 grams	1.848	6.345	1.82–22.13	0.004
2500–4000 grams	0.770	2.161	0.73–6.37	0.163
Birth History				
Cesarean Section	1.348	3.850	2.01–7.39	0.000

From the multivariate analysis above (model fit: Hosmer-Lemeshow p=0.412, indicating good fit), the independent determinants of neonatal hypoglycemia were cesarean delivery (AOR=3.850; 95% CI: 2.01-7.39; p<0.001), low birth weight <2500 g (AOR=6.345; 95% CI: 1.82-22.13; p=0.004), and prematurity <37 weeks (AOR=3.383; 95% CI: 1.59-7.16; p=0.001). Gestational age <37 weeks had a 3.4 times higher risk of hypoglycemia than term infants (37-40 weeks) after adjusting for other variables. Maternal DM and eclampsia, although significant in the bivariate analysis, were not retained as independent predictors in the final model, possibly due to the limited sample sizes in these subgroups (DM, n=9; eclampsia, n=22).

The present study identified a hypoglycemia prevalence of 15.0% among neonates at Dr. Zainoel Abidin Hospital in Banda Aceh. This finding is higher than that reported by Babu et al. (2016), who found a prevalence of 8.2%, but comparable to that of Yunarto & Sarosa (2019), who reported 18.2% at a tertiary hospital in Semarang. The relatively high prevalence in our study likely reflects the case mix of a tertiary referral center, which typically receives a higher proportion of high-risk pregnancies and complicated deliveries.

Bivariate analysis revealed a significant association between gestational age and neonatal hypoglycemia. Preterm infants demonstrated an elevated risk compared to term infants, which aligns with the findings of Chen et al. (2022), who reported that preterm delivery was associated with an increased hypoglycemia risk. The pathophysiological basis for this association is related to inadequate hepatic glycogen reserves and immature gluconeogenic enzyme systems in preterm neonates.

Birth weight was another significant predictor in this study. Both low-birth-weight

and macrosomic infants showed an increased risk of hypoglycemia compared to normal-birth-weight infants. This finding is consistent with that of Zhao et al. (2020), who demonstrated significant associations between abnormal birth weight categories and hypoglycemic episodes.

Regarding maternal age, the bivariate analysis revealed no significant association with hypoglycemia. This finding aligns with investigations performed in Allentown examining term and non-diabetic gestations, which demonstrated that maternal age lacked a meaningful correlation with hypoglycemia. Maternal body weight prior to gestation also showed no significant association in this study.

Maternal diabetes mellitus was significantly associated with neonatal hypoglycemia. This parallels the findings of West et al. (2020), who reported that 28.2% of neonates from mothers with diabetes developed hypoglycemia. Eclampsia also showed a significant bivariate association with hypoglycemia in the present study.

Cesarean section delivery demonstrated the strongest independent association with neonatal hypoglycemia in the multivariate analysis. Ogunyemi et al. (2017) similarly identified cesarean sections as an independent risk determinant. However, confounding by indication should be considered in this study. The underlying mechanism involves preoperative maternal fasting protocols that reduce maternal glucose availability and subsequently diminish transplacental glucose transfer to the fetus (Wu et al., 2023). Additionally, delayed initiation of breastfeeding following cesarean delivery may

Neonatal glycemic homeostasis relies on maternal glycemic status and inherent regulatory mechanisms. Fetal glycogen accumulation begins during the second trimester of gestation. Accordingly, premature neonates develop hypoglycemia due to insufficient glycogen and adipose reserves, immature glycogenolytic and gluconeogenic enzymes, and elevated metabolic requirements resulting from a proportionally larger cerebral mass (Yunarto & Sarosa, 2019; Wu et al., 2023).

Neonates from both diabetic and non-diabetic mothers may develop macrosomia. The pathophysiology involves maternal and fetal hyperglycemia, which precipitates insulin secretion, insulin-like growth factor release, and growth hormone release, inducing augmented fetal glycogen and adipose tissue deposition. Neonates with a birth weight of>4500 g have a 7-fold increased risk of hypoglycemia relative to normal birth weight has been reported (Rekani & Raouf, 2021).

Based on these findings, routine blood glucose screening is recommended for high-risk neonates, particularly those delivered by cesarean section, preterm infants, and neonates with low birth weight. Early feeding initiation within the first hour and enhanced skin-to-skin contact should be prioritized, especially in cesarean deliveries. Close monitoring is also advised for infants born to diabetic or eclamptic mothers.

This study has several limitations, including (1) a single-center retrospective design limiting generalizability; (2) reliance on medical records introducing potential information bias; (3) single glucose measurement possibly causing misclassification; (4) small subgroup sizes for some variables (maternal DM, n=9; obesity, n=7; macrosomia, n=21) limiting statistical power; (5) unmeasured confounders such as feeding type and cord clamping practices; and (6) no neurodevelopmental follow-up to assess long-term outcomes.

Conclusion

This study successfully identified significant risk factors for neonatal hypoglycemia at Dr. Zainoel Abidin Hospital in Banda Aceh. The results demonstrated that cesarean delivery, low birth weight, and prematurity were the most significant independent risk factors for neonatal hypoglycemia. Although maternal diabetes mellitus and eclampsia showed significant associations in the bivariate analysis, neither was retained as an independent predictor in the final model. Based on these findings, routine blood glucose screening should be implemented for high-risk neonates, particularly preterm infants, infants with low birth weight, and those delivered via cesarean section.

Healthcare providers should prioritize early feeding initiation and skin-to-skin contact, especially for infants delivered via cesarean section, to reduce the risk of hypoglycemia. Further prospective studies with larger sample sizes, standardized hypoglycemia definitions, and longitudinal neurodevelopmental follow-

ups are recommended to validate these findings and develop evidence-based clinical protocols specific to the local population.

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