

Neonatal hypoglycemia and associated factors at Wangaya General Hospital

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ABSTRACT

Keywords:

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In the early hours to early days of life, managing low blood glucose levels and screening infants at risk are common problems in the care of newborns. Still missing, though, is a precise definition of newborn hypoglycemia. The purpose of this study is knowing that pregnancy hypertension/preeclampsia/eclampsia, prematurity, small-gestational-weight (SGA), large-gestational-weight (LGA), asphyxia, and sepsis are risk factors associated with neonatal hypoglycemia. The type of research conducted was a cross-sectional retrospective analytic study on infants in the perinatology room at Wangaya Hospital in 2022. The sample in this study consisted of 18 hypoglycemia babies and 18 normoglycemia babies taken by purposive sampling with matching hypertension/preeclampsia/eclampsia pregnancy, prematurity, SGA, LGA, asphyxia and sepsis. Data collection used medical record data and perinatology register data. Statistical tests used were Chi-Square and logistic regression with a 95% confidence interval. The results showed that prematurity was an associated risk factor (OR=2.78; 95% CI=1.437-5.379), asphyxia and sepsis also showed statistical significance (OR=2.07; 95% CI=1.221-3.513) (OR=2.27; 95% CI=1.257-4.109). In multivariate analysis, there was no statistical significance among other factors (p-value 0.019). Prematurity, asphyxia, and sepsis were risk factors associated with the incidence of neonatal hypoglycemia with odds of 2.78 times, 2.07 times and 2.27 times respectively compared to the control population. However, in the multivariate analysis, there was no relationship between one factor to another factor that influenced each other in being a risk factor associated with hypoglycemia at Wangaya Hospital.

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INTRODUCTION

One of the sensitive indicators to assess public health in a country is the health status of infants. Indonesia's health profile in 2021 showed under-five deaths totaling 27,566 of which 73.1% of cases were dominated by neonatal deaths. The most common causes of neonatal deaths in 2021 were asphyxia (27.8%) and low birth weight (LBW) (34.5%) (Kemenkes RI, 2022). Asphyxia and LBW can lead to clinical manifestations in the form of hypoglycemia (Alsalem et al., 2019; Gomella et al., 2004).

The American Academy of pediatrics (AAP) explains that an absolute definition of hypoglycemia as a specific value or range cannot be defined because there are no evidence-based studies that can define clinically relevant neonatal hypoglycemia, but there is agreement by the AAP and the Pediatric Endocrine Society (PES) that there are 2 forms of neonatal hypoglycemia; transitional hypoglycemia that can be resolved in less than 48 hours and persistent hypoglycemia that will continue and is pathological (Gomella et al., 2004). Hypoglycemia is the most common metabolic disorder in the neonatal period (Bhand et al., 2014; Sharma et al., 2017). During the transition from intrauterine to extrauterine life, normal neonates usually have lower plasma glucose concentrations than those that occur later in life (Rozance & Wolfsdorf, 2019). Neonatal hypoglycemia is one of the most common diagnoses requiring intensive care (Gomella et al., 2004; Rozance & Wolfsdorf, 2019).

Neonatal hypoglycemia is most common in the following groups of infants: IUGR, infants born to diabetic mothers, late pre-term infants (34-36 weeks). Infants who experience perinatal stress (e.g., fetal distress, perinatal ischemia, maternal preeclampsia/eclampsia, sepsis, hypothermia) or infants who have congenital heart disease have an increased metabolic energy demand, which puts them at risk for hypoglycemia (Abramowski et al., 2019; Vain & Chiarelli, 2021). Screening of infants at risk and management of low blood glucose levels in the first hours to first few days of life are frequent issues in newborn care (Aziz et al., 2004; Narvey & Marks, 2019). However, a clear definition of neonatal hypoglycemia is still lacking. Current screening guidelines and management algorithms are based on limited evidence, and rely more on expert opinion to provide recommendations.

So based on the background described above and considering the high mortality rate of neonates, the authors would like to conduct further research on factors associated with the incidence of hypoglycemia in neonates at Wangaya Regional General Hospital in 2022. The research would like to give more insight into the discussed issue and better prevention of neonatal hypoglycemia.

METHOD

This cross-sectional study was conducted in Perinatal Unit of Wangaya General Hospital, Denpasar, Bali Indonesia. Data were retrieved from medical record of infants born in 2022, with a sample size of 36 babies. Maternal Hypertension/preeclampsia/eclampsia were defined as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg in pregnancy accompanied by with or without proteinuria and with or without seizure. Preterm was defined as baby born before 37 weeks of pregnancy. Baby born with birthweight more than 2 deviation standard of WHO chart was defined as large-gestational-of-age (LGA) and baby with birthweight below 2 deviation standards of WHO was defined as small-gestational-of-age (SGA). Asphyxia was defined as difficulty of breathing in newborn baby measure by APGAR score below 7 at the 5th minute after birth. Sepsis of newborn was defined as clinically sepsis including septicemia sign. Blood glucose levels was conducted from medical records and were measure from a heel puncture blood sample.

Characteristics of infants, maternal age, delivery methods, maternal pregnancy-related conditions, as well as maternal and neonatal factors were recorded. Newborn babies with congenital anomalies were exclude. The sampling technique was consecutive non-random sampling. Data is secondary data by recording the results of measuring blood sugar levels in the first 24 hours and defined as hypoglycaemia if blood sugar levels below 47 mg/dL. Data were analysed using SPSS 29 for Windows software. Means and proportions of blood glucose levels and basic socio-demographic data, as well as clinical data, were analysed by Chi-square test, and predictive logistic regression respectively. Multivariate analysis was performed to identify significant risk factors related to the occurrence of hypoglycaemia. Results with P values < 0.05 were considered to be statistically significant. The Medical and Health Research Ethics Committee of Wangaya General Hospital approved this study.

RESULTS AND DISCUSSION

The research used a total sample of 36 babies and divided in two groups, 18 babies who were diagnosed with hypoglycemia and the rest with diagnoses other than hypoglycemia. In this study, there were 12 (33.3%) infants with maternal factor of hypertension/preeclampsia/eclampsia. Preterm babies were less than term babies. SGA, LGA, and asphyxia show a fairly small percentage of less than 20% of the total sample.

Based on the results of the analysis, there was a significant relationship between infant factors and the incidence of hypoglycemia. There were statistically significant association between preterm infants and the incidence of hypoglycemia ($p=0.005$), asphyxia ($p=0.044$), and sepsis ($p=0.027$). Meanwhile, other infant factors studied in this study, which are SGA and LGA, were not significantly significant ($p>0.05$). Maternal factors that were studied, which is hypertension/preeclampsia/eclampsia of pregnancy, were not significantly related to the incidence of hypoglycemia. In the multivariate analysis, it was found that only prematurity statistically significantly influenced other variables on hypoglycemia with a value of $p=0.019$.

Neonatal hypoglycemia is a common occurrence during the first few days after birth as infants adapt to the extra-uterine environment. The definition of neonatal hypoglycemia remains a challenge, as infants can be asymptomatic at very low glucose concentrations or show mild symptoms of hypoglycemia (Mitchell et al., 2020).

Previous studies have shown that the incidence of hypoglycemia can be explained by multifactorial factors, which are infant and maternal factors. Maternal factors include gestational diabetes, hypertension in pregnancy, preeclampsia/eclampsia and high BMI. While infant factors that increase the incidence of hypoglycemia are prematurity, small of gestational age (SGA), large of gestational age (LGA) (even without diabetes), infant with diabetic mother (IDM), hypothermia, asphyxia, IUGR, sepsis, erythroblastosis fetalis, polycythemia, transient hyperinsulinemia, stress-induced hyperinsulinemia, HNF4A/HNF1A mutation, and congenital syndrome (Gomella et al., 2004).

In this study, there was a significant association between prematurity and the incidence of hypoglycemia. The relationship was statistically significant with p -value = 0.05. These findings are similar to research by Mitchell et al. (2020) which showed hypoglycemia affects 5-10% of healthy infants, with a higher incidence in premature infants. The fetus does not accumulate glycogen until 27 weeks of age, then accumulates slowly until 36 weeks, and after birth glucose concentrations decrease to a low of 3-3.3 mmol/L in the first 1-2 hours in term infants, term infants use stored glycogen for self-sustained glucose homeostasis. In comparison, preterm infants have lower glycogen stores and deplete them faster, thus are at higher risk of hypoglycemia after birth (Mitanez, 2007).

In contrary to the previous study where maternal hypertension or preeclampsia is one of the risk factors for neonatal hypoglycemia (Mitchell et al., 2020) but this is different with the results of this study, where statistically there is no significant relationship between hypertension/preeclampsia/eclampsia during pregnancy with the occurrence of neonatal hypoglycemia, this is thought to be due to incomplete data, especially not checking blood sugar in the case of infants directly with these risk factors, where the examination is carried out after giving fluids or after starting enteral feeding, so the results of the examination become invalid.

In this study it was also found that the presence of infants at birth with APGAR < 7 was associated with the incidence of hypoglycemia in neonates. It was found that 85.7% of neonates born with asphyxia developed hypoglycemia with p value = 0.044. Similar thing was found in the research of Yunarto and Sarosa (2019). Asphyxia causes an increase in anaerobic glycolysis process along with glycogenolysis which predisposes neonates to hypoglycemia. In contrary to previous studies, in this study there was no significant difference between SGA babies and AGA babies, this finding may be due to the limited number of research samples, as well as unclear time limits when checking blood sugar, so that the results obtained did not show significance (Yunarto & Sarosa, 2019).

LGA is one of the factors causing neonatal hypoglycemia, this is due to hyperinsulinemia during fetal gestation so that it becomes a predisposing factor for hypoglycemia at birth, in a study by Araz et al. (2006) it was stated that the incidence of neonatal hypoglycemia in LGA infants was at higher risk than AGA infants, the current study did not find an association between LGA infants and the occurrence of neonatal hypoglycemia with $p = 0.169$, this is thought to be due to the small population of LGA babies so that the samples obtained are not enough to show the association of LGA babies with hypoglycemia.

This study also found the incidence of sepsis babies with neonatal hypoglycemia, as many as 81.8% of sepsis babies experienced hypoglycemia, this is similar to research by Gupta et al. (2019) which found 39.6% of sepsis babies experienced hypoglycemia. Sepsis conditions can affect blood glucose levels. Newborns who experience sepsis will have difficulty in receiving nutritional intake and this can cause hypoglycemia. Similarly, the increased metabolic demand and hypothermia caused by sepsis can reduce glucose levels (Ahmad & Khalid, 2012).

After conducting bivariate analysis, the variables included in the multivariate analysis criteria were prematurity, LGA, SGA, asphyxia, and sepsis. Multivariate analysis in this study showed that prematurity was statistically significant, but to determine the relationship between factors, at least two variables were needed. The results obtained in this study are not in accordance with several studies, one of which is from Mitchell et al. (2020) which shows an influence between variables. This is thought to be due to the sample size and variables that are too small, so further research with a larger sample size and wider variables will provide different results.

CONCLUSION

Neonatal hypoglycemia is a common occurrence during the first few days after birth, as infants adapt to the extra-uterine environment. Maternal factors include gestational diabetes, hypertension in pregnancy, preeclampsia/eclampsia, and high BMI. Infant factors that increase the incidence of hypoglycemia include prematurity, small of gestational age (SGA), large of gestational age (LGA), infant with diabetic mother (IDM), hypothermia, asphyxia, IUGR, sepsis, erythroblastosis fetalis, polycythemia, transient hyperinsulinemia, stress-induced hyperinsulinemia, HNF4A/HNF1A mutation, and congenital syndrome.

Prematurity was found to significantly influence other variables on hypoglycemia, but the results did not align with previous studies. The presence of infants at birth with APGAR < 7 was associated with the incidence of hypoglycemia in neonates, with 85.7% of neonates born with asphyxia developing hypoglycemia.

LGA, a factor causing neonatal hypoglycemia, is a predisposing factor for hypoglycemia at birth. However, the study did not find an association between LGA infants and the occurrence of neonatal hypoglycemia due to the small sample size and variables. Further research with larger sample sizes and wider variables may provide different results.

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