Difference of Calcium Levels in Infants with Low Birth Weight

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ABSTRACT

Background: Hypocalcemia is a condition that can cause serious disorders, especially in newborns. The occurrence of hypocalcemia is an event that often occurs in babies born that can be caused due to late parathyroid hormone function in calcium metabolism in the baby’s body. Hypocalcemia is often associated with hypotension and disorders of the heart rhythm, symptoms that are often seen are apnea, tachycardia, lethargy, vomiting, and gastrointestinal disorders. This study aimed to analyze differences in calcium level between low birth weight infants.

Subjects and Method: A cross sectional study was conducted at Dr Moewardi Hospital, Surakarta, Central Java, from December 2016 to April 2017. A sample of 158 LBW children was selected using consecutive sampling. The dependent variable is a decrease in calcium levels. The independent variable is low birth weight babies. Data collected by medical records. Data were analyzed using multiple logistic regression.

Results: Calcium level ≥1.13 mmol/L (OR= 0.30; 95% CI= 0.15 to 0.57; p <0.001), no seizures (OR= 0.20; 95% CI= 0.06 to 0.64; p = 0.004), and QoTC (OR= 0.20; 95% CI= 0.07 to 0.572; p= 0.003) decreased the risk of low birth weight.

Conclusion: Calcium level ≥1.13, no seizures, and QoTC decrease the risk of low birth weight.

Keywords: low birth weight, hypocalcemia

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The problem is more common in infants and infants with low birth weight (LBW). Problems that often occur are metabolic disorders, one of which is hypocalcemia (Jain et al., 2008; Ronald et al., 2011).

Hypocalcemia is a condition that can cause serious disorders, especially in newborns. The occurrence of hypocalcemia is an event that often occurs in babies born that can be caused due to late parathyroid hormone function in calcium metabolism in the baby’s body. Baby’s calcium during the womb is actively transferred from the mother’s circulation to the fetus’s circulation through a transplacental calcium pump that is regulated by the hormone parathyroid-related peptide (PTHrP). The majority of fetal calcium transport is increased in the third trimester, this process results in higher calcium concentrations in the fetus compared to the mother which causes hypercalcemia in the fetus, with total calcium concentrations ranging from 2.5 to 2.75 mmol/L and ionized calcium around 1.5 mmol/L that can be measured in umbilical cord blood in term babies (Series I et al., 2005). Hypocalcemia can occur in premature babies, mothers with diabetes, and babies who have asphyxia. Premature infants, hypocalcemia is associated with the cessation of active calcium transport during pregnancy and in asphyxia infants can be caused by renal insufficiency, metabolic acidosis, and secretion of parathyroid hormone (PTH).
when the baby is born thereby reducing plasma calcium levels.

Hypocalcemia is often associated with hypotension and disorders of the heart rhythm, the symptoms that are often seen are apnea, tachycardia, lethargy, vomiting, and gastrointestinal disorders (Brown et al., 2000; Zhou et al., 2009). In newborns it is said hypocalcemia if the total calcium level is below 2.00 mmol/L in term infants, and under 1.80 mmol/L in preterm infants. Mild hypocalcemia if the value of calcium 2.00-2.12 mmol/L can be seen without symptoms, moderate hypocalcemia if the value of total calcium levels is 1.90-2.00 mmol/L, and neuromuscular symptoms can be seen in severe hypocalcemia with calcium levels <1.90 mmol/L (Mimouni et al., 1994; Aggrawal et al., 2008).

SUBJECTS AND METHOD

1. Study Design
This was a cross-sectional study conducted at Dr. Moewardi hospital, Surakarta.

2. Population dan Sample
The study population was infants with birth weight <2,500 grams. A sample of 158 LBW infants was selected by consecutive sampling.

3. Study Variables
The dependent variable of this study birth weight. The independent variables were calcium level, gender, calcium supplement, convulsion, and QoTC.

4. Operational Definition of Variables
Low birth weight was infants born with birth weight <2,500 grams regardless of gestation. Birth weight is the weight of a baby weighed a maximum of 24 hours after birth (Damanik, 2008).

Small for gestational age (SGA) was infants born with birth weights between the 10th and 90th percentiles according to the weight relationship/gestational age. The measurement scale is using a nominal scale

Intra-uterine growth restriction was infants born with birth weight <10th percentile for estimated fetal weight (EFW) according to the Lubchenco chart. Infants with IUGR will be assessed based on birth weight which is then plotted to the Lubchenco body weight/gestational age chart (Damanik, 2014; Gomella, 2013). The measurement scale was continuous.

Hypocalcemia was defined by various restrictions, such as calcium levels less than 1.13 mmol/L. Measurement of calcium levels was carried out using the ion-selective electrode (ISE) method. The samples used are blood and tubes without additional substances. Storage time until inspection is recommended not more than 30 minutes, with a temperature of 15-30°C Celsius. The measurement tool used is the AVL ROCHE 9180 engine.

The QT interval (QoTC) was a measurement made on an electrocardiogram used to assess some of the electrical properties of the heart.

5. Study Instruments
Data collected from medical records and questionnaires.

6. Data Analysis
Univariate analysis describes data in n and% values. The relationship of each independent variable to the dependent variable was analyzed using Chi square.

7. Research Ethic
This study was approved by the Board of Health Research Ethics Commission Dr. Moewardi hospital/Sebelas Maret University School of Medicine Number: 842/X/ HREC / 2016.

RESULTS

A. Univariate analysis
Overall infants had an average birth weight of 1,970 grams (Mean = 1,970.79; SD = 354). Of 158 babies, there were 81 (51.26%) IUGR infants and 77 (48.73%) were SGA infants.
Table 1. Sample Frequency Distribution

| Variable                     | N       | (%)     |
|------------------------------|---------|---------|
| Gender:                      |         |         |
| - Male                       | 83      | (52.53%)|
| - Female                     | 75      | (47.47%)|
| Pregnancy Age:               |         |         |
| - LBW                        | 83      | (52.53%)|
| - VLBW                       | 50      | (31.65%)|
| - ELBW                       | 25      | (15.82%)|
| Calcium Level:               |         |         |
| - ≥1.13 mmol/L               | 85      | (53.80%)|
| - <1.13 mmol/L               | 73      | (46.20%)|
| Calcium Supplement:          |         |         |
| - Yes                        | 45      | (28.48%)|
| - No                         | 113     | (71.52%)|
| Nutrition                    |         |         |
| - Formula                    | 65      | (41.14%)|
| - Breastmilk + human milk fortiﬁer (HMF) | 21 | (13.29%)|
| - Exclusive breastfeeding     | 72      | (45.57%)|
| Convulsions                  |         |         |
| - Yes                        | 61      | (38.61%)|
| - No                         | 97      | (61.39%)|
| QoTC                         |         |         |
| - Yes                        | 82      | (51.89%)|
| - No                         | 76      | (48.11%)|
| Mortality:                   |         |         |
| - Alive                      | 124     | (78.48%)|
| - Dead                       | 34      | (21.52%)|

Table 2. Relationships of calcium levels, sex, calcium supplements, nutrition, QoTC seizures, mortality, and infant birth weight

| Variable                     | SGA  | %    | IUGR  | %    | OR   | p    |
|------------------------------|------|------|-------|------|------|------|
| Calcium Level                |      |      |       |      |      |      |
| <1.13                        | 24   | 32.9 | 49    | 67.1 | 0.30 | <0.001|
| ≥1.13                        | 53   | 62.4 | 32    | 37.6 |      |      |
| Gender                       |      |      |       |      |      |      |
| Male                         | 41   | 49.4 | 42    | 50.6 | 1.06 | 0.431|
| Female                       | 36   | 48.0 | 39    | 52.0 |      |      |
| Calcium Supplement           |      |      |       |      |      |      |
| Yes                          | 11   | 45.83| 14    | 28.57| 2.12 | 0.144|
| No                           | 13   | 54.17| 35    | 71.43|      |      |
| Convulsion                   |      |      |       |      |      |      |
| Yes                          | 14   | 58.33| 43    | 87.75| 0.20 | 0.004|
| No                           | 10   | 41.67| 6     | 12.24|      |      |
| QoTC                         |      |      |       |      |      |      |
| Yes                          | 8    | 33.33| 35    | 71.43| 0.20 | 0.003|
| No                           | 16   | 66.67| 14    | 28.57|      |      |

The average body weight of IUGR infants was 2,044 grams (Mean = 2044.67; SD = 251) and the average weight of SGA infants was 1,896 grams (Mean = 1,896.76; SD = 167). Average
calcium levels (Mean = 1.07; SD = 0.09), with 73 infants (46.20%) experiencing hypocalcemia with serum calcium levels <1.13 mmol/L and 85 infants (53.79%) with normal calcium levels ≥1.13 mmol/L.

**B. The result of bivariate analysis**

Table 2 shows the relationship of calcium levels, sex, calcium supplements, nutrition, QoTC seizures, mortality, and infant birth weight. Table 2 shows that calcium levels ≥1.13 (OR = 0.30; p < 0.001), no seizures (OR = 0.20; p = 0.004), and no QT interval (OR = 0.20; p = 0.003) reduce the risk of birth weight low according to gestational age.

Table 2 showed that female sex (OR = 1.06; p = 0.431) and not getting Ca supplements (OR = 2.12; p = 0.144) increases the risk of low birth weight small gestational age.

**DISCUSSION**

Low calcium levels in IUGR infants are caused by malfunctioning of organs optimally. When the baby is born, active calcium transport during pregnancy will be stopped while in infants with low birth weight often there is renal insufficiency, metabolic acidosis, and secretion of parathyroid hormone (PTH) is less at the time of the baby which can cause a decrease in plasma calcium levels (Horne et al., 2004; Zhou et al., 2009). But in infants with LBW, the amount of glomerulus is still lacking, so that the postnatal renal flow increases, and the Glomerulos Filtration Rate (LFG) decreases. In addition, gastrointestinal tract maturation in LBW infants is also hampered so that calcium absorption through nutrient supply is also less than optimal (Elizabeth et al., 2007; Kamilah et al., 2008).

The newborn babies with SGA suffer from various metabolic problems such as metabolic acidosis, obvious hypoglycemia, hypocalcaemia (Mazumder et al., 2012). A study by Honarpisheh (2003) reported that about 25% of low birth weight infants developed early hypocalcemia. Inadequate dietary intake of calcium may lead to a decrease in serum calcium levels (Peacock, 2010; Kant et al., 2019). Some complications of pregnancy may be associated with lower serum calcium levels e.g. pre-eclampsia during pregnancy, low birth weight, preterm delivery, and neonatal death (Sabour et al., 2006; Hofmeyr et al., 2014).

Chi square test results showed significantly different results in seizure variables and prolongation of the QT interval between hypocalcemia in infants with SGA and IUGR. The results of this study were followed by an analysis looking for Odd Ratio and significant results were squeezed into seizure variables and lengthening the QT interval. The seizure variables were obtained (OR = 0.20; 95% CI = 0.06 to 0.64; p = 0.004) which showed that the incidence of hypocalcemia in infants with SGA was 5.12 times less likely to cause seizures compared to hypocalcemia in IUGR infants. Seizures in neonates arise as a consequence of neural injury, resulting from hypoxia, ischemia, or metabolic disturbances such as hypoglycemia or hypocalcemia (Davis et al., 2010).

Prolongation of QT interval (OR = 0.20; 95% CI = 0.07 to 0.57; p = 0.003) shows that the incidence of hypocalcemia in infants with SMK has a 5 times lower probability of causing prolongation of QT intervals compared with hypocalcemia in IUGR infants. QT (c) and QT (d) in young adults previously born preterm with an ELBW were correlated with gestational age and birth weight (Bassareo et al., 2011).

**AUTHOR CONTRIBUTION**

Sandi Nugraha did the study and wrote the manuscript. Harsono Salimo and Dwi Hidayah wrote the manuscript and suggested the discussion materials.

**CONFLICT OF INTEREST**

There is no conflict of interest in this study.
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