

Percentage birth weight loss and hyperbilirubinemia during the first week of life in term newborns

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Abstract

Background Hyperbilirubinemia is the most common problem in term newborns during the first week of life. Hyperbilirubinemia in term newborns without other risk factors is usually caused by dehydration and reduced calorie intake that is marked by excessive weight loss.

Objective To determine the relationship between percentage birth weight loss and hyperbilirubinemia during the first week of life in term newborns.

Methods A cross sectional study was conducted at the Department of Child Health, Medical School, Udayana University, Sanglah Hospital, Denpasar, Indonesia. The weight of term newborns was measured on the first, third, and seventh day after birth. In addition, a complete blood count, reticulocyte count, and peripheral blood smear, were carried out on the first day. Serum bilirubin level was measured on the first, third, and seventh day. Clinical signs, jaundice, type and frequency of intake, and time of meconium transit were followed during the stay in hospital. Linear regression, correlation, and logistic regression analysis were performed to determine variables related to hyperbilirubinemia.

Results 68 newborns were enrolled in this study, with 7 developed hyperbilirubinemia by the third day. There was a significant ($P < 0.001$) but weak to moderate correlation ($r = 0.39$) between percentage birth weight loss and total serum bilirubin concentration on the third day. Logistic regression analysis showed that percentage birth weight loss on the third day was significantly related to hyperbilirubinemia [OR 38.18 (95% CI 2.29 to 637.61), $P = 0.011$].

Conclusion Percentage birth weight loss is related to hyperbilirubinemia in term newborn during the first week of life. [Paediatr Indones. 2009;49:149-154].

Keywords: birth weight loss percentage, hyperbilirubinemia, term newborn

Hyperbilirubinemia is the most common problem during the early neonatal period.^{1,2} Data from the USA show that approximately 60% of four millions newborns have clinical jaundice each year.³ In 1998, Maisels⁴ found that the prevalence of hyperbilirubinemia was between 8 and 20% during the first week of life. A study in Jakarta showed that neonatal jaundice was found in as many as 14% of normal newborns born by vaginal delivery.⁵ In 1993, Surjono⁶ found that the prevalence of hyperbilirubinemia in term newborns was 11.9% in Yogyakarta, Indonesia. Early discharge of healthy term newborns after delivery makes bilirubin elevation go undetected.⁷ Hyperbilirubinemia can progress to complications such as encephalopathy (kernicterus) although this is rare.⁸ As clinical jaundice is visible when the serum bilirubin level reaches 5–7 mg/dl, it is necessary to use another objective parameter to detect hyperbilirubinemia in healthy term newborns before we measure serum bilirubin level.^{9,10}

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Hyperbilirubinemia in healthy term newborns during the first week of life is caused by elevation of unconjugated serum bilirubin.^{11,12} If other causes of hyperbilirubinemia cannot be identified, this condition may be caused by dehydration due to low calorie and inadequate intake during the first few days after birth. One risk factors for hyperbilirubinemia is excessive weight loss.^{12,13} Normally, a healthy term newborn will lose approximately 4–7% of their birth weight during the first few days of life.¹⁴ The aim of this study was to determine the relationship between percentage birth weight loss and hyperbilirubinemia during the first week of life in term newborns.

Methods

This was a cross sectional study involving healthy term newborns who were delivered at the Perinatology

Division, Department of Child Health, Medical School, Udayana University, Sanglah Hospital, Denpasar, Indonesia, between February 1st and December 31st 2007. We included singleton newborns of ≥ 37 weeks gestation, appropriate for gestational age, delivered vaginally without complication, and with an APGAR score after the first minute after birth of >6 , and were managed at mother's room (rooming-in). Patients were recruited from the Denpasar or Badung area, and parents agreed to join the study and signed informed consent. We excluded babies who developed jaundice in the first 24 hours of life, or if an underlying disease related to hyperbilirubinemia was present (hemolytic disease, blood extravasations, metabolic disease, obstructive intestinal disease). Newborns were also excluded if other complications such as cholestasis, infectious disease, or symptoms related to dehydration (diarrhea, vomiting, fever) were present before discharge, or if

Table 1. Baseline characteristics of study subjects

Characteristics	Hyperbilirubinemia n=7	No Hyperbilirubinemia n=61
Gestational age, weeks, mean (SD)	38.57 (0.79)	39.08 (1.19)
Sex, n		
Male	3	30
Female	4	31
Birth weight, mean (SD) g	3150.00 (448.14)	3095.08
History of jaundice in siblings, n		
Yes	2	2
No	5	59
Intake frequency, UNITS		
First day, mean (SD)	5.28 (1.38)	6.54 (1.31)
< 8x/day, n	6	37
$\geq 8x/day$, n	1	24
Third day, mean (SD)	6.57 (0.79)	8.09 (1.27)
< 8x/day, n	6	16
$\geq 8x/day$, n	1	45
Seventh day, mean (SD)	9.42 (1.81)	10.79 (1.47)
< 8x/day, n	2	3 (4.91)
$\geq 8x/day$, n	5	58 (95.08)
Intake type, n		
Breastfeeding	5	35
Breastfeeding+Formula	2	26
Birth weight loss on day 3, mean (SD)	321.43 (85.91)	155.74 (73.09)
Birth weight loss percentage on day 3, mean (SD)	10.33 (2.68)	5.09 (2.52)
$\geq 10\%$	6	6
< 10%	1	55
Birth weight regain percentage on day 7, mean (SD)	98.57 (1.96)	100.09 (2.10)
< birthweight, n	4	24
\geq birthweight, n	3	37
Meconium transit time, mean (SD) hrs	27.43 (3.41)	26.75 (4.41)
Hb level, mean (SD) g/dl	15.63 (2.46)	15.79 (1.41)
Hematocrit level, mean (SD) %	44.94 (7.86)	45.09 (4.61)

infectious disease, dehydration, hyperbilirubinemia or nutritional problems developed at home before they visited the hospital on the seventh day. In addition newborns were also excluded if blood specimen were unavailable.

The minimal sample size was estimated to be 60, calculated by assuming correlation coefficient of 0.50, $\alpha=0.05$, and power of 90%. Eligible subjects were selected consecutively, and all underwent body weight measurement on the first, third, and seventh day after birth. Complete blood count, reticulocyte count, and peripheral blood smear were measured on the first day, while serum bilirubin levels were measured on the first, third and seventh day. Follow up was carried out to monitor any clinical signs, jaundice, intake types and frequency, and meconium transit time.

Linear regression analysis using scatter plots were generated to determine the relationship between weight percentage and serum bilirubin level on the third and seventh day. We also used Pearson correlation test or alternative to determine the relationship between percentage birth weight loss and serum bilirubin level on the third day. Other variables were analyzed using multivariate analysis. A P value of 0.05 was used to determine significance. This study was approved by the Ethics Committee on Research and Development of Sanglah Hospital, Denpasar.

Results

During the study period, 73 subjects met the inclusion criteria. Three newborns were excluded due to hemolytic anemia, sepsis, and because blood specimens were unavailable. Two newborns were not followed up as they did not return to hospital on the seventh day and they could not be located. The study was completed with a total of 68 newborns. The baseline characteristics and results of the birth weight monitoring of the subjects are shown in **Table 1**.

Table 2. Serum bilirubin level results

Serum bilirubin level	Hyper-bilirubinemia n=7	No Hyperbilirubinemia n=61
Total serum bilirubin level, mean (SD) mg/dl		
First day	6.19 (0.50)	4.84 (1.33)
Third day	15.82 (1.83)	8.77 (1.79)
Seventh day	11.06 (3.89)	5.50 (3.45)
Direct serum bilirubin level, mean (SD) mg/dl		
First day	0.66 (0.25)	0.46 (0.17)
Third day	0.75 (0.42)	0.54 (0.20)
Seventh day	0.85 (0.49)	0.54 (0.29)
Indirect serum bilirubin level, mean (SD) mg/dl		
First day	5.53 (0.48)	4.38 (1.28)
Third day	15.07 (1.77)	8.23 (1.79)
Seventh day	10.20 (3.82)	4.96 (3.28)

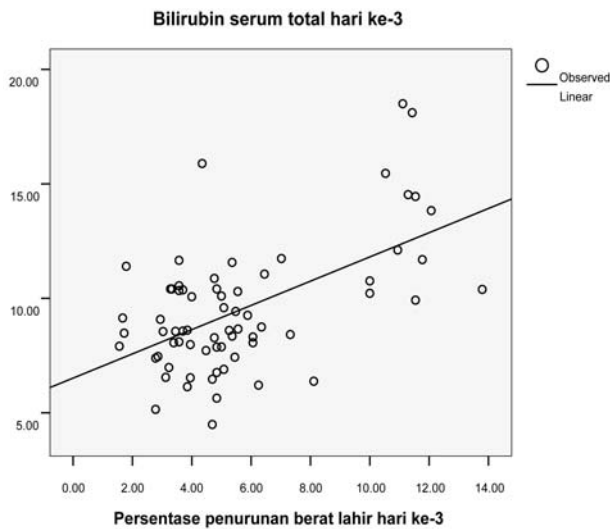


Figure 1. Scatter plot of relationship between percentage birth weight loss and total serum bilirubin level on the third day

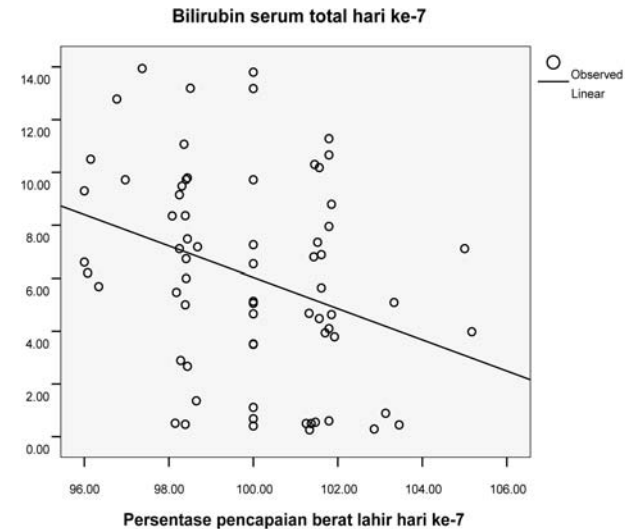


Figure 2. Scatter plot of relationship between percentage birth weight gain and total serum bilirubin level on the seventh day

Table 3. Relationship between other variables and hyperbilirubinemia

Variables	B	SE	Wald	df	P	OR	95% CI
Intake frequency on first day	-17.575	8632.472	0.000	1	0.998	0.000	(0.000;-)
Intake frequency on third day	18.155	8632.472	0.000	1	0.998	76652940	(0.000;-)
Intake type	0.171	0.562	0.093	1	0.761	1.19	(0.39;3.57)
Meconium transit time	0.138	0.148	0.866	1	0.352	1.15	(0.86;1.53)
Percentage birth weight loss on day third	3.642	1.436	6.430	1	0.011	38.18	(2.29; 637.61)

Seven newborns had hyperbilirubinemia by the third day of life, with a total serum bilirubin level of 15.82 (SD 1.83) mg/dl. The data is shown in **Table 2**. Subjects that had hyperbilirubinemia were treated by phototherapy.

Linear regression analysis showed a linear relationship between percentage birth weight loss and total serum bilirubin level on the third day after birth with the regression model $y = 6.52 + 0.53X$, $P < 0.001$ (**Figure 1**), and between percentage birth weight regain and total serum bilirubin level on the seventh day with regression model $y = 65.12 + (-0.59)X$, $P = 0.007$ (**Figure 2**).

Using Spearman correlation analysis, a positive but weak correlation was found between percentage birth weight loss and total serum bilirubin level on the third day with correlation coefficient (r) of 0.39 ($P = 0.001$). A negative weak correlation was found between percentage birth weight regain and total serum bilirubin level on the seventh day with $r = -0.30$ ($P = 0.012$).

Logistic regression analysis of related variables and hyperbilirubinemia showed that only percentage birth weight loss on the third day had significant correlation with hyperbilirubinemia [OR 38.18 (95% CI 2.29; 637.61), $P = 0.011$]. **Table 3** shows the results from the logistic regression analysis.

Discussion

Hyperbilirubinemia is the most common cause of readmission during the early neonatal period.^{7,15,16} Seven newborns in our study (10%) had hyperbilirubinemia on the third day after birth. In 2001 in Italy, Bertini *et al*¹ showed that 112 of 2174 (5.1%) of newborns with a gestational age of ≥ 37 weeks had developed hyperbilirubinemia by 72 hours after birth, with total serum bilirubin level of ≥ 12.9 mg%. Another study performed in China by Ding, *et al*¹⁷

in 2001 found that as many as 34.4% of 875 term newborns had a total serum bilirubin level of ≥ 12.9 mg%. In 1993, Surjono, *et al*⁶ used prospective observational study in Yogyakarta that found that by the fifth day as many as 11.9% term newborns had a total serum level bilirubin of ≥ 12.9 mg% or an unbound bilirubin level of ≥ 0.5 μg .

The mechanism of physiological jaundice is multifactorial, and must be differentiated from pathological jaundice.¹⁸ Jaundice that is related to breastfeeding between the second and fourth days after birth is known as breastfeeding jaundice, breast "non-feeding" jaundice, or breastfeeding-associated jaundice, and is due to enhancement of enterohepatic bilirubin circulation.^{16,18} The precise mechanism still unknown, but it is thought to be related to reduced calorie intake that stimulates an increase in enterohepatic circulation of bilirubin. Another underlying mechanism may be that reduced calorie intake will lead to a reduction in clearance of unconjugated serum bilirubin.¹⁸

Reduced calorie intake during the first few days after birth is indicated by excessive weight loss.^{16,18,19} Weight loss of more than 7% to 10% is considered as pathological and is a sign of dehydration and reduced calorie intake.²⁰⁻²² Our study shows that there was a significant but weak linear relationship between percentage birth weight loss and total serum bilirubin level on the third day after birth with $r = 0.39$ ($P = 0.001$). Logistic regression analysis also showed that percentage birth weight loss on the third day was significantly related to hyperbilirubinemia [OR 38.18 (95% CI 2.29 to 637.61), $P = 0.011$]. Bertini, *et al*¹ also found that term newborns with hyperbilirubinemia had a significant birth weight loss [264.49 (SD 74) gram], compared with the loss for all subjects in the study [214.63 (SD 146) gram] ($P < 0.001$), and that birth weight loss was significantly associated with hyperbilirubinemia on the third day ($P < 0.05$).

In the multicenter study performed by Ding *et al*¹⁷ it was found that total serum bilirubin level in

the first week was significantly associated with birth weight loss ($P < 0.001$) in term newborns. A case control study in term newborns by Gale *et al*²³ in Israel found that a high level of serum bilirubin was significantly associated with high percentage birth weight loss ($P < 0.05$). Salariya and Robertson²⁴ also found a significant relationship between birth weight loss and hyperbilirubinemia in healthy term newborns ($P < 0.01$) during the early neonatal period. Maximum birth weight loss occurred on the second day after birth and birth weight regain found on the fifth day.

In contrast, Sarici, *et al*²⁰ found no significant difference between hyperbilirubinemia and non-hyperbilirubinemia in newborns during the first week of life when the percentage birth weight loss was $\geq 10\%$ ($P = 0.672$). This result may be because their subjects were near term newborns rather than term newborns as in our study. Surjono⁶ performed a prospective observational study on 196 term newborns that were delivered vaginally and were exclusively breastfed. The newborns were followed until the fifth day after birth. They found no significant difference between the hyperbilirubinemia group and non-hyperbilirubinemia group ($P > 0.05$). Differences in that study compared with ours, such as all subjects being exclusive breastfed and the use of the student's *t* test, might lead to different results. Our study found weak negative correlation between percentage birth weight regain and total serum bilirubin level on the seventh day with $r = -0.30$ ($P = 0.012$), but the relationship between these two factors is still unknown.

Many other factors are related to hyperbilirubinemia during the first week of life of term newborns, including intake, prolonged meconium transit time, or delay of meconium evacuation.^{13,16,25} However, our study showed that intake frequency, intake type, and meconium transit time are not related to hyperbilirubinemia. Bertini *et al*¹ found that infants with supplementary feeding (breastfeeding + formula) had a greater significant birth weight loss [266 (SD 150) gram] compared with other types of intake (breastfeeding = 200.33 (SD 145) gram, formula = 207.2 (SD 70) gram [$P < 0.01$]). Another study²⁴ found a significant difference of intake type and meconium transit time ($P < 0.0001$), while Yamaguchi and Yamanouchi²⁶ found that frequent feeding had a significant relationship with meconium evacuation frequency ($P < 0.01$), weight loss ($P < 0.01$) and

hyperbilirubinemia ($P < 0.05$) on the sixth day after birth.

To conclude, our study shows that percentage birth weight loss by the third day is the only factor that is independently associated with hyperbilirubinemia in normal term newborns delivered vaginally. Adequate intake should be ensured and weight loss should be monitored in all newborn babies in the first few days of life.

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